Jai Raman *Editor*

Management of Heart Failure



Volume 2: Surgical

Springer

Management of Heart Failure

Management of Heart Failure

Volume 2: Surgical

Edited by

Jai Raman
University of Chicago, Chicago, USA

DropBooks

Springer

Jai Raman, MBBS, MMed (Syd), FRACS, PhD (Melb)
Professor of Surgery
Director of Adult Cardiac Surgery
University of Chicago
Chicago, IL, USA

ISBN: 978-1-84800-103-9 e-ISBN: 978-1-84800-104-6
DOI: 10.1007/978-1-84800-104-6

British Library Cataloguing in Publication Data

Management of heart failure
Vol. 2: Surgical
1. Heart failure - Treatment
I. Raman, Jai
616.1'2906

ISBN-13: 9781848001039

Library of Congress Control Number: 2008920050

© Springer-Verlag London Limited 2008
Apart from any fair dealing for the purposes of research or private study, or criticism or review, as permitted under the Copyright, Designs and Patents Act 1988, this publication may only be reproduced, stored or transmitted, in any form or by any means, with the prior permission in writing of the publishers, or in the case of reprographic reproduction in accordance with the terms of licences issued by the Copyright Licensing Agency. Enquiries concerning reproduction outside those terms should be sent to the publishers.
The use of registered names, trademarks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant laws and regulations and therefore free for general use.
The publisher makes no representation, express or implied, with regard to the accuracy of the information contained in this book and cannot accept any legal responsibility or liability for any errors or omissions that may be made.
Product liability: The publisher can give no guarantee for information about drug dosage and application thereof contained in this book. In every individual case the respective user must check its accuracy by consulting other pharmaceutical literature.

Printed on acid-free paper

9 8 7 6 5 4 3 2 1

Springer Science + Business Media
springer.com

On June 4, 2007, a small plane carrying the University of Michigan thoracic organ transplant team crashed into Lake Michigan, soon after takeoff from Milwaukee, Wisconsin. These were the members of that team and they epitomize many unsung heroes who make up the teams that work in the field of heart failure and transplantation:

Dr Martinus “Martin” Spoor, a cardiac surgeon who had been on the faculty since 2003 at the University of Michigan.

Dr David Ashburn, a fellow in pediatric cardiothoracic surgery.

Richard Chenault II, a transplant donation specialist with the university transplant program.

Richard Lapensee, a transplant donation specialist with the university transplant program.

DropBooks

Dennis Hoyes, a Marlin air pilot.

Bill Serra, a Marlin air pilot.

This publication is dedicated to their memory. We would like to dedicate these two volumes of the book to the many healthcare givers of various persuasions who look after patients and facilitate the delivery of care. We also dedicate this effort to the numerous pioneers in the realm of heart failure research and development.

Preface

As I sit here, thinking about the field of heart failure, what springs to mind are the unsung heroes who pervade the arena. Right from transplant coordinators to rehabilitation therapists, from heart failure cardiologists to transplant surgeons, critical care physicians to transplant pharmacists, etc. All this becomes more personal, in light of the recent plane crash in the mid-west of the USA, when an entire team from the University of Michigan lost their lives after they had harvested a set of thoracic organs. Even more poignant was the fact that Dr Martinus Spoor, who contributed to a chapter in this book, lost his life in that crash. Therefore, this is dedicated to his memory and many more like him who have not been widely recognized.

Let us start with transplantation of the heart itself. Even though Christiaan Barnard set the world on fire with the successful heart transplant in 1967, it was the hard work of people like Norman Shumway who over the years built the science and many teams that made cardiac transplantation a success. In the same vein, the tireless efforts of Vincent Dor should not go unsung. I remember many meetings when he would get up and present his data on geometric left ventricular reconstruction. The initial skepticism of the audience gave way to credulous acceptance only over a period of two decades. It is remarkable that the patience and persistence of pioneers like him, secure in their clinical and scientific observation, have paved the way for other practitioners to follow. This has helped in the formation of heart failure as a specialty. When one considers that Billroth exhorted in the late 1800s that surgery on the heart was foolhardy and dangerous, it is amazing that coronary artery surgery became the most commonly performed surgical procedure toward the end of the twentieth century. However, as less invasive options of angioplasty and stenting became more widespread, more and more patients were able to survive heart attacks. These patients then had more attention paid to their cardiovascular risks and longevity improved. The cost of all this improved survival is heart failure of varying degrees. So much so, that heart failure is the most common DRG code for hospital admissions in the developed world. The emergence of heart failure as a specialty began with acceptance of heart transplantation and the use of immunosuppression. However, alternative and delaying techniques to transplantation along with better drug therapy have built this whole specialty into a multidisciplinary behemoth. We have a range of options in the therapy of heart failure, ranging from medications to special techniques of resynchronization, venous ultrafiltration, beating heart surgery, etc.

Coronary artery surgery numbers declined but patients who now present for bypass surgery invariably have some degree of left ventricular dysfunction and more diffuse disease. They are often on aspirin and plavix. As survivors of major and minor cardiac events, these veterans of hospital admissions and multiple interventions pose great management challenges that require coordination between a multitude of caregivers and practitioners.

As the teams that look after these complex patients grow, so do the number of unsung heroes who perform tirelessly to improve the outcomes of these sick patients. Remember, all this happens

while the media is constantly talking about new stem cell therapies, new robotic operations, new drugs for heart failure, etc. Very little mention is made about the nitty-gritty and daily grind of mundane tasks such as cardiac rehabilitation after a heart attack or cardiac surgery that dramatically improves the well-being of heart failure patients. Few lay people know about the existence of perfusionists who run the heart lung machine in open heart surgery or manage those large ventricular assist devices that keep patients alive. The ensemble approach of having a team look after patients for various aspects of care in a coordinated fashion has resulted in many of these patients doing well.

My task here is therefore to acknowledge all those unsung heroes around the world and thank them for their work. I would also like to thank all the contributors to this book, which is the first two-volume effort in the realm of heart failure. Grant Weston deserves credit, as the editor from Springer who had the foresight to hang his shingle on a "higher than usual risk" publication. No doubt there are areas of these two volumes that could be improved upon or updated, but our aim was to provide a good overview of the Comprehensive Management of Heart Failure.

Jai Raman
Chicago, IL
October 2007

DropBooks

Contents

Preface vii

Contributors xi

1 Surgical Perspectives 1
Jai Raman

2 Pathophysiology—Clinical Spectrum and Current Management 11
Mahesh P. Gupta and Jai Raman

3 Strategies in Surgical Management 23
Irving L. Kron, R. Ramesh Singh, James D. Bergin, and Benjamin B. Peeler

4 Advanced Heart Failure: Transplant vs Nontransplant Surgical Options 41
Stephen Westaby and Gabriele Bertoni

5 Transplantation for End-Stage Heart Disease 71
David C. McGiffin and James K. Kirklin

6 OPCAB Treatment for Heart Failure 99
Mercedes Dullum and Jai Raman

7 Circulatory Support for Bridging to Recovery or Transplantation 111
Francis D. Pagani

8 Left Ventricular Reconstruction in Ischemic Cardiomyopathy 137
Salim Aziz, Constantine Athanasuleas, and Jai Raman

9 Modifications of the Dor Procedure and Failure Modes of the Procedure 153
Jai Raman

10 Mitral Valve Repair 161
Yoshikazu Suzuki, Martinus T. Spoor, and Steven F. Bolling

11 Destination Therapy with Permanent Mechanical Circulatory Assist Devices 181
Murali Macherla and Valluvan Jeevanandam

12 Enabling Techniques and Technologies 193
Patricia Gramling-Babb, Valluvan Jeevanandam, Jai Raman, David Song, Hilton M. Hudson II, and John Paul Williams

13 Catheter-Based and Surgical Therapy for Ventricular Tachycardia 215
Bradley P. Knight, J. Massen, Gil Bolotin, and Jai Raman

14 Catheter Ablation for Atrial Fibrillation in Patients with Heart Failure 221
Bradley P. Knight

15 Surgical Therapy for Atrial Fibrillation 225
G. Bolotin and J.G. Maessen

16 Pacing Therapies, Defibrillators, and Post-Operative Arrhythmias 233
Bradley P. Knight

17 Ventricular Containment, Shape Change, and Infarct Restraint 239
Jai Raman

18 Other Techniques in Special Circumstances: Pulmonary Thromboendarterectomy in Right Heart Failure 251
Michael M. Madani and Stuart W. Jamieson

19 Surgical Management of Pediatric Heart Failure and Heart Failure due to Congenital Heart Disease 263
Emile A. Bacha

20 Anesthetic Management and Hemodynamic Management 269
Mark A. Chaney

21 Perioperative and ICU Care, Fluid Management, and Renal Support 279
Rinaldo Bellomo and Patrick Murray

22 New Therapies and What Is on the Horizon 297
Keiichi Tambara and Masashi Komeda

Index 307

DropBooks

Contributors

Salim Aziz, MD
Clinical Professor of Surgery, George Washington University, Washington DC, USA

Emile A. Bacha, M.D.
Department of Cardiac Surgery, Children's Hospital Boston, Boston, MA, USA

Rinaldo Bellomo, M.D.
Department of Intensive Care and, Austin Hospital, Melbourne, VIC, Australia

James D. Bergin, M.D.
Department of Heart Failure and Heart Transplantation, University of Virginia Health Sciences Center, Charlottesville, VA, USA

Gabriele Bertoni, M.D.
Department of Cardiothoracic Surgery, John Radcliffe Hospital, Oxford, UK

Steven F. Bolling, M.D.
The University of Michigan, Section of Cardiac Surgery, Taubman Health Care Center, Ann Arbor, MI, USA

Gil Bolotin, M.D., Ph.D.
Department of Cardiac Surgery, Rambam Medical Center, Haifa, Israel

Mark A. Chaney, M.D.
Department of Anesthesia and Critical Care, University of Chicago, Chicago, IL, USA

Filippo Civaia, M.D.
MRI and CT Scan Department, Centre Cardiothoracique de Monaco, Monte-Carlo, Monaco

Vincent Dor, M.D.
Department of Thoracic and Cardiac Surgery, Centre Cardiothoracique de Monaco, Monte-Carlo, Monaco

Mercedes Dullum, M.D.
Department of Cardiothoracic Surgery, Vleveland Clinic Florida, Weston, FL, USA

A. Eker, M.D.
Department of Thoracic and Cardiac Surgery, Centre Cardiothoracique de Monaco, Monte-Carlo, Monaco

Patricia Gramling-Babb, M.D.
Chief of Cardiac Anesthesia, Jacksonville Medical Center, Jacksonville, Florida, FL, USA

Mahesh P. Gupta, Ph.D.
Department of Cardiac and Thoracic Surgery, The University of Chicago, Chicago, IL, USA

Hilton M. Hudson II, M.D.
Department of Cardiothoracic Surgery, Franciscan Physicians Hospital, Munster, IN, USA

Stuart W. Jamieson, M.B., F.R.C.S.
Division of Cardiothoracic Surgery, University of California San Diego Medical Center, San Diego, CA, USA

Valluvan Jeevanandam, M.D.
Department of Cardiothoracic Surgery, University of Chicago, Chicago, IL, USA

James K. Kirklin, M.D.
Surgery and Cardiothoracic Transplantation, University of Alabama at Birmingham, Birmingham, AL, USA

Bradley P. Knight, M.D.
Department of Cardiac Electrophysiology, University of Chicago, Chicago, IL, USA

Masashi Komeda, M.D., Ph.D.
Department of Cardiovascular Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Irving L. Kron, M.D.
Department of Surgery, University of Virginia Health Sciences Center, Charlottesville, VA, USA

Murali Macherla, M.D.
Cardiothoracic Surgeon, Albuquerque, NM, USA

Michael M. Madani, M.D.
Department of Cardiothoracic Surgery, University of California, San Diego, CA, USA

J. G. Maessen, M.D.
Chief of Cardiothoracic Surgery, University of Maastricht, The Netherlands

Komeda Masashi
Department of Cardiovascular Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

David C. McGiffin, M.D.
Department of Surgery, University of Alabama at Birmingham, Birmingham, AL, USA

Francois Montiglio, M.D.
ICU of Cardiothoracic Surgery, Centre Cardiothoracique de Monaco, Monte-Carlo, Monaco

Patrick Murray, M.D.
Department of Medicine, Section of Nephrology,University of Chicago Hospitals, Chicago, IL, USA

Francis D. Pagani, M.D., Ph.D.
Department of Surgery, University of Michigan Medical Center, Ann Arbor, MI, USA

Benjamin B. Peeler, M.D.
Department of Surgery, University of Virginia Health Sciences Center, Charlottesville, VA, USA

Jai Raman, M.B.B.S., M.Med. (Syd), F.R.A.C.S., Ph.D. (Melb)
Department of Cardiac Surgery, University of Chicago, Chicago, IL, USA

Mohamed Saab, M.D.
Department of Thoracic and Cardiac Surgery, Centre Cardiothoracique de Monaco, Monte-Carlo, Monaco

Michael Sabatier, M.D.
Department of Thoracic and Cardiac Surgery, Centre Cardiothoracique de Monaco, Monte-Carlo, Monaco

R. Ramesh Singh M.B., BCh, A.F.R.C.S.I.
University of Virginia Health Sciences Center, Charlottesville, VA, USA

David Song, M.D.
Department of Plastic Surgery, University of Chicago, Chicago, IL, USA

Martinus T. Spoor, M.D.†
The University of Michigan, Section of Cardiac Surgery, Taubman Health Care Center, Ann Arbor, MI, USA

Yoshikazu Suzuki, M.D.
Section of Cardiac Surgery, Department of Surgery, University of Michigan Cardiovascular Center, Ann Arbor, MI, USA

Keiichi Tambara, M.D., Ph.D.
Department of Cardiovascular Surgery, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Stephen Westaby
Department of Cardial Surgery, John Radcliffe Hospital, Oxford, UK

John Paul Williams, M.D.

DropBooks

1
Surgical Perspectives

Jai Raman

1.1. A Brief Overview of the History and Evolution of Surgical Treatment of Heart Failure

This chapter focuses on the early history of surgical procedures to address heart failure, right from mitral valve surgery to left ventricular aneurysm surgery and then onto transplantation. There is a brief outline of the early history of heart failure. A current view of the growing field of heart failure surgery and the expanding armamentarium of surgical therapies in heart failure is mentioned.

Diseases desperate grown By desperate appliance are relieved,/Or not at all. (Shakespeare: Hamlet 4. 3. 9)

The earliest mention of heart failure was by Sushruta, in 600 BC, a prominent physician and surgeon of ancient India. There is a good description of what we now describe as heart failure, with patients manifesting with dyspnea, cough, wheezing, and edema. In his treatise known as *Sushruta Samhita*, he saw these as symptoms of a special derangement of a special organ system related to "pittam" or circulating fluids and prescribed emetics, diuretics, and purgatives for its treatment.[1]

1.2. Western Tradition

Within the Western medical tradition, Lancisi (1654–1720) laid the foundation for contemporary understandings of the pathology of heart disease. In particular, he described the "aneurysm of the heart," which would now be termed dilatation, and recognized the swelling of neck veins as pathognomonic of right heart dilatation.

Albertini (1672–1733) of Bologna, a pupil of the great physician Malphigi, was the first physician to realize the importance of dyspnea as a symptom of heart disease. Morgagni (1682–1771), a professor of anatomy at Padua, recognized and anatomically distinguished between the two chief forms of cardiac enlargement: dilatation and hypertrophy. He also deduced that dyspnea and asthma could have cardiac causes, connecting these symptoms to right heart failure in particular. Senac (1693–1770), a French physician, was the first to write about the importance of inflammation as a cause of heart disease. He described thrills that were associated with valvular insufficiency. Laennec (1781–1826) invented the stethoscope in 1819 and regarded dilatation and hypertrophy to be the most important cardiac lesions. William Stokes (1804–78) recognized the importance of the myocardium and analyzed its relationship to valvular disease.[2]

1.3. Frank–Starling Relationship

In 1895, Otto Frank, a famous German physician, showed the importance of cardiac filling and size in governing its contractility. In 1915, E. H. Starling demonstrated conclusively the relationship of preload and cardiac filling to cardiac contraction and performance in an experimental heart–lung preparation. This was called "Starling's law of the heart" and was the basis of the Frank–Starling curve or relationship. The Frank–Starling curve is a plot of cardiac size and contractility.[3] *This curve or law*

is the very basis of defining the limits of ventricular dilatation and the decompensation that occurs when the heart enlarges beyond a certain size.

The present emphasis on the medical management of modern heart failure is not that much different. The last few decades have seen great strides in the development of devices and surgical procedures in the treatment of heart failure. However, very little of this is known to the wider medical community, let alone the cardiac surgical fraternity. Heart failure has often been called the final surgical frontier. However, this is not quite true as the history of cardiac surgery will attest….

Cardiac surgery is a relatively young surgical specialty that is now in a stage of flux. The heart was always held in great reverence. The great Viennese surgeon Theodor Billroth asserted in the 1880s that it might be dangerous to contemplate surgery on the heart.

In the European tradition, the first surgical treatment of heart failure was drainage of a pericardial effusion that was unresponsive to diuretics, performed by Francisco Romero in Aragon around 1814. Dominique Larrey, surgeon to Napoleon's Imperial Guard, drained a traumatic pericardial effusion presenting as tamponade in 1814.

Dr. Daniel Hale Williams, an African-American surgeon who set up the Provident Hospital not far from the campus of the University of Chicago, performed the first repair of a cardiac wound in a patient called James Cornish, in 1893. Dr. Daniel Hale Williams called for six of his fellow black physicians to help him get the dying man into an operating room. Carefully making an incision along the fifth rib, Williams exposed the man's still-beating heart and his near-fatal wound. Williams and his surgeons evaluated and sewed up a small but ragged gash located on the surface of the heart between two coronary arteries and closed the pericardium. This is very pertinent to this book, which was conceived and produced at the University of Chicago when the first major cardiac procedure was performed in an affiliate hospital. This fact is even more poignant, because both authors of this chapter have been on the faculty of this university (Figure 1.1).

There were two similar instances in Europe around the same time. In 1894, Ansel Cappelen sutured a 2-cm laceration on the surface of the ventricle, at the University of Oslo, Norway. His patient remained gravely ill succumbing 4 days later.



FIGURE 1.1. Daniel Hale Williams, credited with the first repair of a cardiac wound, Provident Hospital, Chicago, 1893.

Ludwig Rehn at the University of Frankfurt am Main, in1896, is credited with carrying out the first successful repair of a large cardiac wound with a surviving patient.

The early decades of the twentieth century set the tone for cardiac surgery, especially in patients with heart failure as a consequence of rheumatic stenosis of the mitral valve.

1.4. Pioneers of Heart Surgery

In 1902, Lauder Brunton wrote a remarkably prescient but restrained paper entitled "Preliminary Note on the Possibility of Treating Mitral Stenosis by Surgical Methods." Sir Brunton, working at St. Bartholomew's Hospital in London, studied a variety of instruments that could be introduced through the ventricle or the auricle. He also proposed that the commissures be divided rather than the leaflets. Inspite his great vision and extensive cadaver work, supporting his work, the paper set off a flurry of critical letters. The prevailing view of the cardiologists was skeptical and claimed that the prognosis of the condition depended on

the state of the heart muscle rather than on the size of the mitral orifice. Things have not changed that much more than a hundred years later! Unfortunately, it took almost 50 years to prove Brunton's predictions.

Elliot Cutler, across the Atlantic at the Peter Bent Brigham Hospital, Boston, worked with many types of cutting instruments. On May 20, 1923, he operated on a bedridden patient who survived for 4½ years, but could not be sure how much relief of mitral stenosis there was. The subsequent experience with the various cutting procedures of the mitral valve failed because the focus was on cutting the leaflets rather than the commissures.

It was 23 years after Brunon's paper that Henry Souttar introduced a finger through the atrial appendage to ostensibly free up a stenosed mitral valve, on May 6, 1925; to his surprise, he found a regurgitant valve, but established the principle of finger fracture.

In 1910, Alexis Carrel reported on experiments performed at the University of Chicago and at the Rockefeller Institute, New York, at the American Surgical Association. He described a relatively safe period of vena caval occlusion or of cross-clamping of the heart, making it "feasible to cut a mitral or triscuspdian valve, or to perform the curettage of endocardiac vegetations" (Figure 1.2).



FIGURE 1.2. Alexis Carrel, pioneer of cardiac surgical techniques, vascular anastomoses, transplant techniques.

Billroth was not alone, for most of history, the human heart has been regarded as an organ forbidden to surgeons. World War II changed a lot of surgical attitudes. Pioneering advances in antibiotics, anesthesia, and blood transfusions were made by military doctors, who faced injury and suffering on a massive scale (Figure 1.3).

Dr. Dwight Harken, as a young US Army surgeon, was one of the first surgeons to use these improved techniques to gain access to the heart. Many of Harken's patients were young soldiers evacuated from the European front with shell fragments and bullets lodged inside their hearts. Leaving shrapnel wounds could be very dangerous, while removing them could be fatal. Using animal experimentation, he tried to develop a technique that would allow him to cut into the wall of a still-beating heart, insert a finger, locate the shrapnel, and remove it. All of his first 14 animal subjects died. Of the second group of 14, half died. Of the third group of 14, only 2 died. Harken used these techniques in his patients with no deaths, proving that the human heart could be operated upon.

It was not long before surgeons began wondering if Harken's technique might be applied to defective heart valves. In 1947, Harken performed a repeat of the Cutler procedure which resulted in death of the patient. In 1948, within days of each other, Harken and Dr. Charles Bailey, of Philadelphia, independently reported on successful closed mitral commisurotomy using valvulotomes and carefully designed knives. Across the Atlantic, Russell Brock at the Brompton Hospital, London, utilized Souttar's approach of finger fracture through the left atrial appendage with very good results. Dubost in Paris devised a reliable mechanical dilator which was subsequently modified by Oswald Tubbs in South Africa in 1955. This was the early evolution of valvular reparative surgery for heart failure—a truly international effort which provided dramatic relief to a desperately ill group of patients with mitral stenosis.[4]



FIGURE 1.3. Dwight Harken, pioneer cardiothoracic surgeon.

In the ensuing years, dramatic strides were made in anesthesia, cardiopulmonary support, valve replacement, myocardial protection, etc. to facilitate modern cardiac surgery.

1.5. Developments in the Twentieth Century

In terms of the development of cardiovascular surgery, Alexis Carroll, a very innovative researcher, pioneered many of the concepts that helped make contemporary heart surgery possible, including cardiac and other solid organ transplantation.[5] Much of his early work was at the University of Chicago and he continued his work at the Rockefeller Center in New York. It is a great testament to this surgical pioneer that he persevered even though he was not granted a license to practise medicine in the USA!

Following on from Carroll's pioneering work, many groups and stalwarts developed various aspects of heart surgery. In Stanford, California, Shumway and coworkers worked tirelessly to help make cardiac transplantation a reality.[6] Eventually, the introduction of Cyclosporin A helped make transplantation viable.[7]

In relation to the development of other surgical options for treating congestive heart failure (CHF), Chachques and coworkers,[8] working in Paris in the mid-1980s, used an interesting discovery in skeletal muscle transformation to try to improve the function of the failing heart. The left latissimus dorsi muscle was harvested with its intact neurovascular pedicle, wrapped around the heart, and transformed over a period of 10 weeks to a fatigue-resistant state. This technique, known as dynamic cardiomyoplasty, provided some relief to patients with heart failure, but was bedeviled by major morbidity. In addition, the muscle transformation took too long and could impact on the condition of a patient with severe cardiac failure. The mechanism by which this technique worked was probably through containment of the dilating ventricle.

Dr. Randas Batista, a charismatic surgeon from Brazil, first burst on the international scene in 1997 with his ventricular volume reduction surgery.[9] Although his eponymous procedure is not used much any more, he showed the world the value of reducing the size of dilating ventricles to smaller sizes. Batista's technique reduced wall stress and alleviated symptoms in the short term. Unfortunately, the majority of the patients had recurrent ventricular dilatation and either died or proceeded to transplantation.

Another approach that has had some impact on the surgical management of CHF is that of Dr. Steven Bolling and his associates from Ann Arbor, Michigan. They believe that mitral regurgitation is the process by which many patients with heart failure decompensate and manifest clinically. This group advocates radical mitral annuloplasty and has produced reasonably good results with this technique.[10]

Patients with heart failure as a consequence of ischemic heart disease often have large areas of myocardial scarring, some of which may be dyskinetic or truly aneurysmal. Dr. Vincent Dor of Monaco has long advocated a careful reconstruction of the left ventricle in patients with aneurysmal or

DropBooks

dyskinetic segments.[11] These techniques modified linear repairs of ventricular aneurysms advocated by Dr. Denton Cooley.[12] Cooley himself later on employed a patch repair of large aneurysms.[13] Dor's work in the early 1990s demonstrated that excision of these maladaptive scars and implantation of a patch along with a purse string suture to reduce the size of the neck of the aneurysms, in order to reconstruct the ventricle and reduce its size, have beneficial effects.[14] Jatene's contributions to addressing septal dyskinesis have also contributed to improving outcomes with these reconstructive procedures.[15] At centers in Melbourne, Australia, and Chicago, USA, we have also had encouraging results using another modification of Dor's technique,[16] whereby the purse string suture is avoided but a small tailored patch is used in an attempt to reconstruct the ventricle in a smaller and more normal shape. Dr. Patrick McCarthy, at the Cleveland Clinic, has had encouraging results using a modification of Dr. Dor's technique,[17] whereby he uses a large purse string but avoids a patch. Yacoub and coworkers have also looked at using left ventricular assistance to aid recovery of the failing heart.[18]

The most dramatic and eye-catching development was, of course, the first heart transplant. Despite years of work and development by many researchers in the USA and Europe, the first implant was carried out in the Southern Hemisphere well away from those crucibles of development and discovery. In December of 1967, Dr. Christiaan Barnard, at the Groote Schuur Hospital, South Africa, transplanted the heart of a 23-year-old woman killed in a motor vehicle accident into the chest of a middle-aged man. He lived for 18 days, until the powerful drugs used to suppress rejection weakened him and he died of pneumonia. The second patient to receive a heart transplant, at the hands of Dr. Adrian Kantrowitz in the USA, lived only 6 h. Dr. Barnard's next heart transplant patient lived for 18 months.

These surgical triumphs proved short lived as patients began dying of either rejection or infection. By 1971, 146 of the first 170 heart transplant recipients were dead. Transplantation of the heart received bad press and, worse, a bad rap.

Only one surgeon continued—the recently deceased Dr. Norman Shumway persisted in pursuing this high-risk procedure. Throughout the 1970s, he built a team of scientists and doctors to tackle the complex biological problem of tissue rejection in a careful, scientific manner. He developed techniques of endomyocardial biopsies to monitor rejection. It was only fair therefore that Shumway benefited from a chance discovery made in another part of the world.

The soil of Norway's Hardaanger fjord yielded a fungus which allowed the development of cyclosporin, a calcineurin inhibitor that revolutionized organ rejection without knocking out all resistance to infection. Hospitals around the world began to reopen their heart transplant units and their patients began to survive and prosper.

1.6. Congestive Heart Failure

1.6.1. Introduction

Heart failure is a commonly used term that encompasses a wide spectrum of diseases and a range of etiologies. However, in all these cases, the underlying common feature is the presence of some degree of failure of[19] the musculature of the heart to work efficiently. Heart failure may be defined in clinical as well as physiological terms:

CHF is a clinical syndrome rather than a specific disease. CHF is characterized by a reduction in exercise tolerance, poor quality of life, and shortened life expectancy. Hypertension and valvular heart disease were at one time the most common causes of progressive heart failure. However, with an ageing population, ischemic heart disease and diastolic dysfunction have become important causes of heart failure. As the heart dilates, there is increased wall stress. The Frank–Starling curve becomes inapplicable and the increase in diameter makes the heart expend more energy to pump the same amount of blood to maintain a cardiac output prior to dilatation. Physiologically speaking, failure of the heart as a pump is termed as overall heart failure and differs from myocardial failure, which is a reduction in myocardial contractility.[20] One useful way to define heart failure is to state that it exists when the heart is unable to pump sufficient blood to meet the metabolic needs of the body at normal filling pressures, provided the venous return to the heart is normal.

1.7. A Brief Perspective

In general, the survival rate of patients with heart failure is related to their degree of myocardial failure, whereas their symptoms are related more to CHF and its compensatory mechanisms. Most patients with heart failure, however, have an "enlarged heart," which, in technical terms, is due to dilatation of the ventricles. Ventricular dilatation usually runs a progressive course that is variable and predisposes the owner of the heart to sudden cardiac death. Indeed, in a landmark paper, White showed that ventricular volume was a major determinant of survival after myocardial infarction.[20] There are numerous possible causes of overall heart pump failure (Table 1.1).

This large variation in the causes and mechanisms of heart failure has made research into this area difficult. Research has been further hindered by a lack of large animal models that are both appropriate for studying human heart failure and reproducible, reliable, and stable for long-term study.

CHF is the only cardiovascular disorder that is increasing in prevalence, despite important gains made in other cardiovascular arenas. In the USA and other industrialized nations, CHF is reported to be the most common cause for medical hospitalization for patients older than 65 years. It is also distinguished as the leading cause of morbidity and mortality in industrialized nations. Great strides have been made in improving the symptoms of patients and reducing mortality. However, according to noted researchers, patients with CHF are deemed to be "destined to suffer considerable disability and die from their disease."[22]

Table 1.1. Common causes of Heart Failure[21]

Coronary artery disease
Dilated cardiomyopathy of unknown cause
Dilated cardiomyopathy of known cause:
• Hypertensive
• Toxic
• Viral
• Parasitic
Valvular stenosis or regurgitation, with or without left ventricular dysfunction
Hypertrophic cardiomyopathy
Restrictive cardiomyopathy
Pericardial disease
Pulmonary hypertension
Congenital heart disease
High output states
Uncontrolled tachycardia

1.8. The Magnitude of the Problem

The American Heart Association reports that more than 5 million people in the USA have CHF and that at least 550,000 new cases develop on an annual basis. In the USA, in 2001, 6.5 million hospital days were associated with CHF admissions. In that year, 53,000 patients died with CHF as their primary diagnosis. Once patients were hospitalized, heart failure also accounted for 12–15 million visits to the physician during that same period.[23] In 1995, heart failure accounted for more than $10 billion a year in health care costs in the USA.[23,24] Further analysis of costs revealed that when both federal and nonfederal hospital expenditures were examined, the total cost was more like $40 billion for 1994, in the USA.[25]

While better treatment has evolved over the past two decades for ischemic heart disease, only modest improvement has been made in the management of heart failure. The incidence of heart failure is said to double in each decade of life from the age of 45 to the age of 75 years. Thirty-four percent of patients die within the first year of newly diagnosed CHF. Eighty-two percent of men die within 6 years of the diagnosis. In the second to sixth years of diagnosis, death rates associated with CHF are four to eight times that of the general population. However, worsening symptoms are not always a prelude to death. Forty-four percent of deaths in patients with CHF are sudden, with no markers for prediction. The rate of sudden death in this patient group is five times that of the general population.[26]

1.9. Incidence and Prevalence

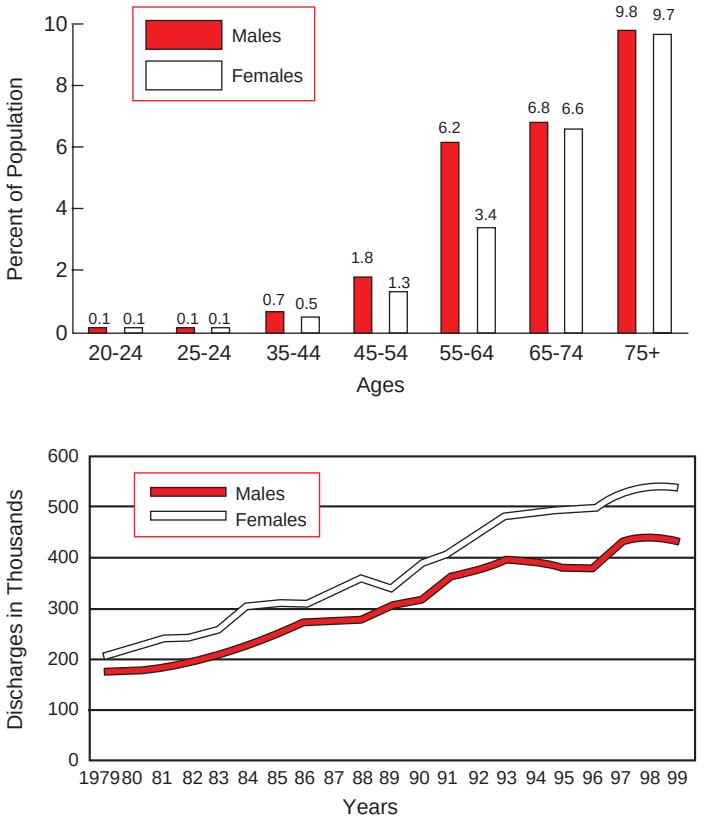
Incidence data on CHF in Australia are estimated at 300,000 patients or 1–2% of the population. In the USA, data on incidence are based on estimates from the study in Framingham, Massachusetts, funded by the National Heart, Lung, and Blood

DropBooks

Institute. The incidence of CHF is equally frequent in men and women, with an annual incidence approaching 10 per 1,000 population after 65 years of age. There is an incidence five times greater in patients who have had a myocardial infarction compared with those who have not. *CHF is the biggest cause of medical admissions in the USA*.

Similarly, prevalence data are not available for Australia, but can be roughly extrapolated from the figures in the USA. However, the Australian Institute of Health and Welfare estimates that heart failure accounts for 5% of all deaths from cardiovascular disease and 10% of all hospitalizations for cardiovascular conditions. However, patients over the age of 65 years accounted for 86% of heart failure admissions.[27]

Close to 5 million Americans have CHF, with an equal representation of the sexes across this figure. CHF is present in 2% of people aged 40–59, in more than 5% of people aged 60–69, and in 10% of people over the age of 70. The prevalence of CHF has also increased steadily over the past 20 years as the population ages[24] (Figure 1.4).



* Hospital discharges include people both living and dead.

Source: CDC/NCHS and the American Heart Association.

FIGURE 1.4. Prevalence of heart failure and hospital discharges of CHF.

1.10. Course of the Disease and Present Treatment Options

Initially, the heart tends to compensate by increasing the heart rate—causing hypertrophy of myocardial cells—and also starts dilating to cope with the load. Eventually, however, these mechanisms fail and the heart continues to dilate. It may enlarge asymptomatically for a variable period of time. As a result, the patient may present quite late, with a certain amount of irreversible cardiac dilatation.[25] The extent of symptoms depends on the clinical phase of the illness; the level of compensation or decompensation; the underlying cause; and aggravating factors, such as a chest infection or a sudden fluid overload. The majority of patients are managed with medications, which provide symptomatic relief but do nothing to stop the underlying process. Patients are often managed with a combination, or "cocktail," of medications that need to be carefully monitored and regularly adjusted. In addition to symptomatic relief, some of these drugs may have significant side effects. However, with progressive myocardial dilatation, drugs become ineffective and the only solution may be surgical therapy of some sort.[28]

The gold standard for treatment of end-stage heart failure is orthotropic cardiac transplantation. This is an expensive therapy and is limited severely by the lack of availability of donor organs. Patients who undergo transplantation must remain on immunosuppressive therapy for life, with the consequent risk of infection, rejection, and graft atherosclerosis.

A variety of other surgical options, such as coronary artery bypass graft surgery, dynamic cardiomyoplasty, radical mitral annuloplasty, and left ventricular volume reduction surgery, have been tried with inconsistent results and variable success. Left ventricular aneurysm repair or infarct exclusion is a technique that is effective for patients with large infarcted segments that are dyskinetic. Apart from these procedures, few surgical options have been developed to deal with CHF. The field is thus ripe for the development of new approaches.

The next chapter deals with the pathophysiology, clinical spectrum, and management of heart failure. That will set the stage for the evolution of the other chapters in this book.

Key Points to Remember

- The first recorded instance of a successful repair of a cardiac wound was by Dr Daniel Hale Williams, at the Provident Hospital, Chicago in 1893.
- Many of the fundamentals and technical advancements are based on the pioneering work of Dr Alexis Carrel, conducted between 1904 and 1912, in Chicago and New York.
- Modern cardiac surgery had its beginnings in addressing heart failure from mitral valve disease.
- However, surgery for heart failure is a newer frontier, following from the success of cardiac transplantation.
- Heart failure is the most common reason and DRG (diagnosis related group) for hospital admissions in the developed world.
- Currently, a range of procedures can be performed with excellent results in patients with heart failure.

DropBooks

References

1. Bhishagratna KL. *Sushruta Samhita* [in English]. Vol. 1. Varanasi, India: Chowkhamba Sanskrit Series Office; 1991.
2. Moon RO. Heart disease. In: Bett WR, ed. *A Short History of Some Common Diseases*. Oxford University Press, Oxford, UK; 1934:109-114.
3. West JB, ed. *Best and Taylor's Physiological Basis of Medical Practice*. 12th edn. Williams & Wilkins, Philadelphia, PA; 1990:227.
4. Shumacker HB. *The Evolution of Cardiac Surgery*. Bloomington, Indiana: Indiana University Press; 1992.
5. Garrion FH. *An Introduction to the History of Medicine*. 4th edn. WB Saunders, Philadelphia, PA; 1960:733-734.
6. Lower RR, Dong EJ, Shumway NE. Long-term survival of cardiac homografts. *Surgery*. 1965;58:110.
7. Borel JF, Feurer C, Gubler HU, Stahelin H. Biological effects of cyclosporine A: A new lymphocytotoxic agent. *Agents Actions*. 1976;6:468.
8. Chachques JC, Grandjean PA, Tomassi JJ, et al. Dynamic cardiomyoplasty—A new approach to assist chronic myocardial failure. *Life Support Syst*. 1987;5:323-326.

9. Batista RJV, Santos JLV, Takeshita N, et al. Partial left ventriculectomy to improve left ventricular function in end-stage heart disease. *J Card Surg*. 1996;11:96-97.
10. Bach DS, Bolling SF. Early improvement in congestive heart failure after correction of secondary mitral regurgitation in end-stage cardiomyopathy. *Am Heart J*. 1995;129:1165-1170.
11. Dor V, Saab M, Coste P, Kornaszewski M, Montiglio F. Left ventricular aneurysm: A new surgical approach. *J Thorac Cardiovasc Surg*. 1989;97:11-19.
12. Cooley AD, Collins HA, Morris GC, Chapman DW. Ventricular aneurysm after myocardial infarction: Surgical excision with use of temporary cardiopulmonary bypass. *JAMA*. 1958;167:557-560.
13. Cooley DA. Repair of post-infarction aneurysm of the left ventricle. In: Cooley DA, ed. *Cardiac Surgery: State of the Art Reviews*. Vol. 4, No. 2. Philadelphia: Handley and Belfus; 1990:309.
14. Dor V, Sabatier M, DiDonato M, et al. Efficacy of endo-ventricular patch plasty in large post infarction akinetic scars and severe left ventricular dysfunction: Comparison with a series of large dyskinetic scars. *J Thorac Cardiovasc Surg*. 1998;116:50-59.
15. Jatene AD. Left ventricular aneurysmectomy. *J Thorac Cardiovasc Surg*. 1985;89:321-331.
16. Raman JS, Sakaguchi G, Buxton BF. Outcome of geometric endo-ventricular repair in impaired left ventricular function. *Ann Thorac Surg*. 2000;70:1127–1129.
17. McCarthy PM, Young JB, Starling RC, et al. Anterior infarct exclusion surgery for ischemic cardiomyopathy. *Circulation*. 1999;100(18, suppl I):514.
18. Suzuki K, Murtuza B, Suzuki N, Smolenski RT, Yacoub MH. Intra-coronary infusion of skeletal myoblasts improves cardiac function in doxorubicin induced heart failure. *Circulation*. 2001;104(12, suppl I):I213-I217.
19. Ross J Jr. Assessment of cardiac function and myocardial contractility. In: *Hurst's "The Heart."* 8th edn. McGraw Hill, New York, 1994:chap 23.
20. White HD, Norris RM, Brown MA, Brandt PWT, Whitlock RML, Wild CJ. Left ventricular end-systolic volume as the major determinant of survival after recovery from myocardial infarction. *Circulation*. 1987;76:44-51.
21. Packer M. Treatment of congestive heart failure. In: Willerson JT, ed. *Treatment of Heart Diseases*. Gower Medical Publishing, London, New York; 1992:chap 2.
22. Guidelines for the evaluation and management of heart failure. Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Evaluation and Management of Heart Failure). *Circulation*. 1995;92:2764-2784.
23. AHA–ACC Practice guidelines on the management of heart failure. 2005.
24. Parmley WW. Cost-effective management of heart failure. *Clin Cardiol*. 1996;19:240-242.
25. Linzbach AJ. Heart failure from the point of view of quantitative anatomy. *Am J Cardiol*. 1960;5:370-382.
26. O'Connell JB, Bristow MR. Economic impact of heart failure in the United Sates: Time for a different approach. *J Heart Lung Transplant*. 1994;13: S107-S112.
27. Australian Institute of Health & Welfare. Heart failure. 2003: Available at: http://www.aihw.gov.au/cvd/major-diseases/heartfailure.
28. Faulkner S, Stoney W, Alford W, et al. Ischemic cardiomyopathy: Medical versus surgical treatment. *J Thorac Cardiovasc Surg*. 1977;74:77-82.

2
Pathophysiology—Clinical Spectrum and Current Management

Mahesh P. Gupta and Jai Raman

2.1. Pathophysiology

The noted biological and medical writer Lewis Thomas mused in his 1983 essay, entitled 'The Artificial Heart':

We do not really understand the underlying mechanism of cardiomyopathies at all, and we are not much better at comprehending the biochemical events that disable the heart muscle or its valves in other more common illnesses. But there are clues enough to raise the spirits of people in a good many basic science disciplines, and any number of engrossing questions are at hand awaiting answers. The trouble is that most of the good questions that may lead, ultimately, to methods for prevention (for example, the metabolism and intimate pathologic changes in a failing myocardium, the possible roles of nutrition, viral infection, blood-clotting abnormalities, hypertension, life-style, and other unknown factors) are all long-range questions, requiring unguessable periods of time before the research can be completed. Nor can the outcome of research on any particular line be predicted in advance; whatever turns up as the result of science is bound to be new information. There can be no guarantee that the work will turn out to be useful. It can, however, be guaranteed that if such work is not done we will be stuck forever with this insupportably expensive, ethically puzzling, halfway technology, and it is doubtful that we can long afford it.[1]

Sixteen years later Willerson observed in an editorial on heart failure that it is 'Not yet clear is what mediates the progression of heart failure after the initial injury, and how it may be influenced'.[2]

In order to understand more fully the mechanisms through which the process of ventricular containment is useful for the treatment of congestive heart failure (CHF), it is crucial to have a thorough knowledge of the pathophysiology of this common heart disease. In this chapter I discuss the disease processes of CHF at a biochemical, molecular or cellular level, and at a more systemic level.

2.1.1. Initiation of Heart Failure

Initial injuries or insults to the myocardium may sometimes be sub-clinical, thus producing immediate signs of heart failure only in a small group of patients. These injuries often initiate a process that leads to chronic CHF over a period of months or years. Three main forces that initiate the process of CHF are

- intrinsic myocardial damage
- abnormal load on one (particularly the left ventricle) or both ventricles
- extrinsic forces affecting the heart.

Over half the cases of intrinsic myocardial damage are due to ischaemia and/or infarction caused by ischaemic heart disease.[3] Myocardial damage resulting in heart failure may also be caused by auto-immune injury, infections, metabolic insults and toxic conditions.[4] Idiopathic dilated cardiomyopathy may be due to self-directed antibodies to myocyte antigens. Immunodulation may cause improvement in these patients.[5] Toxic and metabolic causes include alcohol toxicity and hyperthyroidism.

Abnormal loads on the myocardium may be due to chronic pressure overload (e.g. systemic arterial hypertension) or volume overload (e.g. aortic and mitral valve regurgitation).

DropBooks

Extrinsic causes of heart failure include constrictive pericardial disease, tachycardia-induced heart failure, and 'high-output' heart failure due to severe anaemia or a large arteriovenous fistula or shunt.

2.1.2. Progression

The underlying mechanism in the development and progression of heart failure involves an initial insult followed by ventricular remodelling. A destructive cycle is set in motion whereby the remaining normal myocardium undergoes changes in cellular metabolism, leading to hypertrophy and fibrosis. This gradually results in changes in the ultra-structure of the ventricles through a process called remodelling. Remodelling occurs initially as an adaptive response to improve cardiac performance. Unfortunately over time this response becomes counterproductive and maladaptive.[6]

2.1.3. Molecular and Cellular Basis

There are various factors that impact on the ventricles at a cellular level. For instance systemic arterial hypertension causes a reactivation of embryonic growth factors, which are normally dormant in the adult heart. These factors accelerate protein synthesis and myocyte growth, resulting in hypertrophy of the ventricle.[7] Diastolic dysfunction ensues and progresses to systolic dysfunction, which ends up causing a large, dilated, poorly functioning ventricle.

Myocardial infarction (MI) is another trigger for ventricular remodelling. The irreversibly injured myocardium loses contractile function, causing compensatory changes in the remaining myocardium. This functional overload on non-infarcted muscle, as well as intrinsic changes in the infarcted area (such as myocyte filament slippage), leads to remodelling. This process finally results in a dilated heart with severe dysfunction.[8]

The contributing mechanisms to ventricular remodelling are complex and not completely understood. Current hypotheses focus on certain cytokines and growth factors, such as tumour necrosis factor (TNF).[9] Elevated levels of TNF are found in the myocardium of patients with heart failure. Raised levels of TNF may cause myocyte dysfunction through a mechanism involving the induction of nitric oxide synthase (iNOS).[10,11]

While the maladaptive changes of heart failure can be reversed by successful treatment if instituted early enough,[12] further cellular changes result in apoptosis—programmed cell-death—and fibrous replacement in normal areas of the heart, causing permanent functional damage.[13]

The common end result of chronic congestive failure is systolic dysfunction, which translates as an inability of the left ventricle to eject its contents in systole. Left ventricular ejection fraction while a relatively weak prognostic indicator if used alone[14] is the most frequently used objective estimate of heart failure severity.

Diastolic dysfunction exists when the left ventricle is unable to fill at a normal rate and to a normal extent.[15] Systolic function may be normal in some patients with diastolic dysfunction. This condition can be caused by a variety of conditions, including severe left ventricular hypertrophy, restrictive infiltrative myocardial disease and constrictive pericarditis. There is no accurate way of quantifying diastolic dysfunction. Diastolic dysfunction can be difficult to treat effectively and may progress steadily.[16]

2.1.4. Maladaptive Systemic Responses

Chronic CHF starts off as adaptive cardiac and systemic responses in an attempt to maintain normal perfusion of systemic organs. These responses become counterproductive over time, leading to the progression of heart failure, with worsening symptoms (Figure 2.1).

Various homeostatic mechanisms are activated in CHF, such as the activation of the renin–angiotensin–aldosterone system. Decreased renal perfusion is detected by receptors in the renal arterioles, leading to renin release from the kidneys. The increased angiotensin II that is formed acts on efferent arterioles increasing glomerular filtration pressure, despite reduction in renal perfusion pressure. Aldosterone synthesis is stimulated by angiotensin II, causing retention of salt and water by the kidney. Initially, this mechanism works to preserve normal systemic and renal perfusion. However, over a longer period this process leads to edema, elevated pulmonary artery pressures and increased after-load.[17] Figure 2.2 illustrates these mechanisms.

Figure 2.2 shows that there is an increase in sympathetic activity, as well as vasopressin and renin

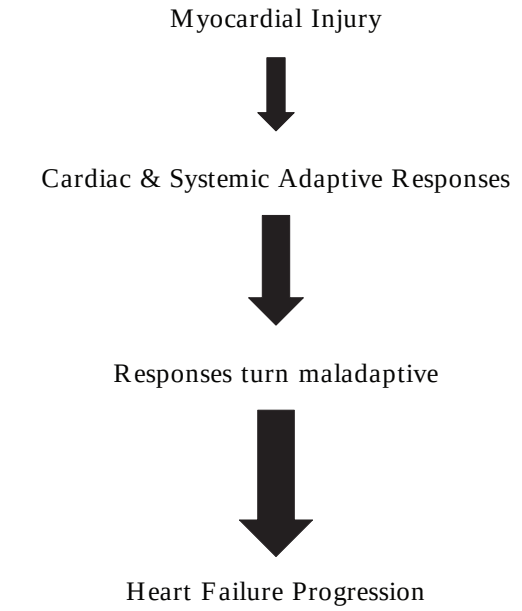


FIGURE 2.1. Mechanism of heart failure progression.

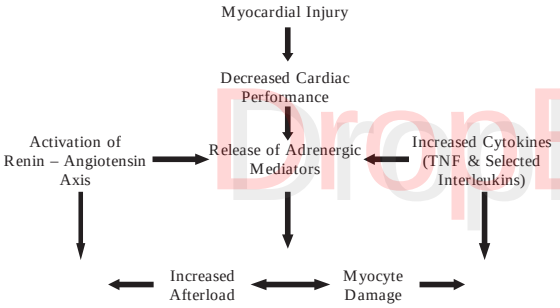


FIGURE 2.2. Cycle of heart failure progression, interacting with the renin–angiotensin axis, adrenergic system and cytokines.

release, in CHF. Neuro-endocrine activation is manifested by the release of norepinephrine, vasopressin and atrial natriuretic peptide.[18] The increased afterload and myocyte damage leads to a repetitive cycle of decreasing cardiac performance. Norepinephrine increases systemic vasoconstriction, chronotropy and inotropy by direct cardiac stimulation.[19] Over time, this increase in tissue norepinephrine activity predisposes to ventricular arrhythmias and sudden cardiac death. Higher circulating levels of plasma norepinephrine have been shown to negatively correlate with the prognosis of heart failure.[20] These values, while a rough guide, can be highly variable and unreliable compared to local concentrations of norepinephrine within the heart. The levels of norepinephrine in the cardiac circulation are measured by norepinephrine spill-over, and are elevated in CHF, providing an accurate prognostic guide.[21]

Increased levels of endothelin are also found in CHF, promoting peripheral vasoconstriction, myocyte hypertrophy and adverse remodelling.[22] Furthermore, atrial and brain natriuretic peptides (ANPs & BNPs) are released by the atria in response to stretch and increased atrial pressure. Neurohormones, cytokines and nitric oxide all interact together in complex ways to create the syndrome of chronic heart failure.

2.1.4.1. Fetal Gene Activation During Heart Failure

In a hypertrophied heart, myocytes are not only big in size but they also have additional sarcomeres. The manner in which these sarcomeres are added depends upon the type of load being imposed on myocytes. In situation of pressure overload, sarcomeres are added in parallel, leading to increased LV wall thickness, whereas during volume overload, they are added in series, resulting in dilation of the ventricular cavity. There are also qualitative differences in sarcomeres of hypertrophied myocytes. A great body of evidence suggest that hypertrophy of myocytes is associated with induction of a group of genes, which are usually expressed during fetal heart development. These genes include activation of β-myosin heavy chain (MHC), skeletal-α-actin and atrial natriuretic factor and the repression of α-MHC and SR-CaATPase. These changes may be initially salutary for an overloaded heart; however, prolonged hypertrophy leads to myocyte dysfunction, which eventually results in heart failure. Results collected from animals studies have also indicated that the loss of α-MHC content is a critical determinant of the reduced myocardial contractility during heart failure. Direct evidence in support of a causal link between the loss of α-MHC and the development of heart failure came from experiments in which the α-MHC gene was ablated. Data correlating even small decrements of α-MHC content with changes in the intrinsic contractile characteristics of the myocardium also support the idea that a critical level of α-MHC content is essential for the normal pump function of the heart.

DropBooks

Another possible cause of a decrease in contractile protein function is an alteration in the expression and/or activity of regulatory proteins. In animal models of heart failure, there are changes in the myosin light chain and the troponin–tropomyosin complex. Changes in myosin light-chain isoforms have been observed in heart samples of patients subjected to increased mechanical stress, and the expression of troponin-T splice variants was found to be altered in failing human myocardium. Changes in the phosphorylation status of Troponin-I have also been suggested to be involved in the loss of contractile activity of myocytes during heart failure. Moreover, defects in sarcoplasmic reticulum Ca^{2+}ATPase and Ca release channels have been suggested to be responsible for the contractile dysfunction of myocytes.

2.1.4.2. Myocyte Cell-Death During Heart Failure

It has been realized that in addition to muscle gene dysregulation, cardiomyocyte cell-death significantly contributes to loss of ventricular function in a failing heart. During increased workload, myocytes undergo a hypertrophic growth response to compensate for the increased demand, the initiating events of which are similar to those that drive cell cycle progression in proliferating cells. A continuous growth signal in myocytes, at some point, causes cells to malfunction and leads to cell-death. As cells die, the work load on the remaining cells increases, which further aggravates this process and eventually leads to organ failure. Both in humans and animals with different cardiac disorders, including ischaemic heart disease, idiopathic dilated cardiomyopathy, hypertensive heart disease, viral myocarditis, pacing-induced cardiomyopathy and different transgenic models of heart failure, myocyte cell-death has been implicated as a common cause of the cardiac pathology. However, the mechanism of cell-death in a failing heart remains highly disputed. Some studies have documented a role of caspases in myocyte cell-death; however, others have disputed this notion. The activation of caspases in ischaemic heart disease seems fairly accepted, but its participation in non-ischaemic diseases remains controversial. Our own studies have shown that in pressure-overloaded hearts Poly ADP Ribose Polymerase (PARP), a nuclear enzyme mediating DNA repair is not cleaved, a marker of caspase-dependent cell-death, but rather its expression is progressively increased in relation to the degree of cardiac hypertrophy, suggesting that haemodynamic stress endangers cardiac myocytes through a mechanism that appears different from the conventional caspase-mediated apoptosis. Activation of PARP has been seen during different animal models of heart failure as well as in failing human hearts. Recent evidence suggests that prevention of cardiomyocyte cell-death by PARP inhibition and/or by changing the activity of other cell-death intermediates protects the overloaded heart from going into failure.

2.1.5. Genetics of Heart Failure

Before we proceed to a discussion of the complex clinical manifestations of CHF, a brief discussion of the genetic factors at work in CHF is necessary for completion. Almost 20% of patients with dilated cardiomyopathy are likely to have an inherited genetic defect. For instance, familial hypertrophic cardiomyopathy is caused by a number of gene mutations affecting β-MHC, cardiac troponin-T and I, alpha tropomyosin, myosin-binding protein C and myosin light chains 1 and 2.[23] In certain conditions such as Duchenne muscular dystrophy, there are definite genetic associations of an abnormal gene called dystrophin with abnormal myocardial function.[24]

2.2. Clinical Spectrum

Heart failure is usually defined as the inability of the heart to generate an output sufficient to meet the metabolic requirements of the body. The left or right ventricles may fail individually or together. Heart failure may also occur in the face of normal systolic ventricular function.

Left heart failure presents with shortness of breath, which, if severe, will occur at rest. Patients are graded on their functional capacity depending on the level of activity that induces shortness of breath. This functional classification, known as the ‘New York Heart Association (NYHA) classification’, is widely accepted and used around the world. This functional classification is used in the assessment of patients, prognostication and in tailoring management. The classes are as follows Table 2.1:

TABLE 2.1. New York Heart Association (NYHA) classification.

NYHA Class I	Shortness of breath on unaccustomed exertion. Normal exercise tolerance.
NYHA Class II	Shortness of breath on accustomed exertion, e.g., breathlessness on walking uphill or climbing a flight of stairs.
NYHA Class III	Shortness of breath on mild exertion, e.g., symptomatic on walking a few metres.
NYHA Class IV	Symptomatic at rest or on minimal exertion.

Minor impairment of cardiac function may remain asymptomatic but as compensatory mechanisms become maladaptive, the clinical features of heart failure emerge. These relate primarily to the consequences of elevated atrial pressures and reduced cardiac output, expressed as congestion and peripheral hypoperfusion, respectively. Manifestations of left and right heart may occur separately, but in reality they often occur together in varying degrees, resulting in the broader syndrome of CHF.

2.2.1. Acute Left Heart Failure

This is usually caused by acute MI, but may also be due to acute aortic or mitral regurgitation, or fulminant myocarditis. The patient usually presents with sudden onset of breathlessness and may cough up pink, frothy sputum. These clinical features are hallmarks of acute pulmonary oedema although, in reality, most patients are now diagnosed on the basis of 'wet lungs' using chest x-ray. Systemic hypoperfusion supervenes, progressing to hypotension, oliguria and, in severe cases, cardiogenic shock.

2.2.2. Chronic Left Heart Failure

Patients usually have varying degrees of dyspnoea on exertion, the causes of which are many. For example, the elevation of left atrial pressure with exertion may be caused by

- respiratory muscle fatigue,
- metabolic factors such as acidosis and renal impairment or
- muscle fatigue due to low cardiac output and poor muscle conditioning.

Clinical examination may reveal signs of low cardiac output and reflex sympathetic stimulation, which include tachycardia, cool peripheries and, occasionally, cyanosis. Auscultation may reveal inspiratory crackles at lung bases, although this can be unreliable; they are just as likely to be retained secretions within the lungs. Pleural effusions may be present. A third heart sound may be present producing a gallop rhythm. In severe heart failure, dilatation of the cardiac base and fibroskeleton causes mitral annular dilatation and mitral regurgitation. This is manifested by a pan-systolic murmur at the apex.

2.2.3. Acute Right Heart failure

Acute right heart failure may be caused by pulmonary embolism or right ventricular infarction. Patients usually present with breathlessness, systemic hypotension, cool skin, elevated jugular venous pressure and occasionally an enlarged liver.

2.2.4. Chronic Right Heart Failure

In this condition patients complain more of fatigue, and breathlessness is common. They also complain of a bloated feeling in the abdomen and a loss of appetite. This may be due to ascites, liver congestion and edema of the gastro-intestinal tract. On examination the jugular venous pulse (JVP) is elevated. Occasionally there may be large 'v' waves in the JVP along with pulsatile hepatomegaly, suggestive of functional tricuspid regurgitation. In such patients a pan-systolic murmur can be heard at the left sternal edge. Peripheral edema and ascites may be present. Occasionally patients present with jaundice and impaired protein synthesis, due to chronic impairment of liver function.

2.2.5. Complications

A variety of cardiac arrhythmias occur in heart failure, especially atrial fibrillation which causes varying degrees of haemodynamic deterioration. Ventricular arrhythmias occur later in the course of the disease and are more sinister, often causing sudden death. Arrhythmias and cardiac dilatation predispose to thrombus formation within cardiac chambers, which can then embolise into the

DropBooks

pulmonary or systemic circulations. Chronic congestion of the lungs also provides a fertile ground for chest infections. Deep vein thromboses as a result of sluggish flow in the veins of the legs and pelvis may progress to pulmonary embolism and sudden death.

Advanced heart failure also causes progressive failure of major organs such as the liver and kidneys.

2.2.6. Diagnosis

As I have described CHF can present with a variable clinical picture. However, a variety of investigations can help confirm the diagnosis, such as electrocardiogram (ECG), chest X-ray, echocardiography, cardiac catheterization, radionuclide ventriculography (RNVG), magnetic resonance imaging (MRI) and cardio pulmonary exercise testing. Such investigative tools are useful for mapping the course and progression of the disease.

2.3. Current Treatment Options for CHF

CHF is a complex medical condition requiring therapeutic interventions at multiple levels. It is the most common cause of medical admissions in Australia, the United States, Canada and the UK. The biggest advance in the treatment of heart failure has been the establishment of 'Heart Failure Clinics' and heart failure groups in hospitals, serviced by people interested in investigating, understanding and managing heart failure.[25]

Multi-disciplinary heart failure programmes that run cardiac rehabilitation courses after MI or cardiac surgery have been effective in reducing heart failure-related admissions.[26] Symptomatic improvement has also been noticed, along with reduced hospitalisation in patients with cardiomyopathy who attend a specialised clinic.[27]

Prevention also plays a very important role. The West of Scotland Study showed that primary prevention, by advocating drug therapy with pravastatin, prevented MI and reduced the incidence of heart failure in a population at risk.[28] The 4S Study (Scandinavian Simvastatin Survival Study) followed patients with coronary artery disease, some of whom were randomly assigned to a placebo group and some to a group treated with simvastatin. Secondary prevention in the 4S Study showed that occurrence of heart failure at 5-year follow-up was significantly higher in the placebo than in the simvastatin group.[29]

Exercise programmes to improve general fitness and the level of exercise tolerance have been shown to significantly improve the functional status of patients with heart failure.[30] Bed rest, which was a cornerstone of traditional therapy for CHF, is therefore no longer advocated for these patients.

Despite these improvements in treatment and prevention, the effective management of heart failure continues to be a pressing concern. Before discussing my research into the utility and efficacy of ventricular containment, this next section will review current approaches to the treatment of CHF, both medical and surgical.

2.3.1. Drug Therapy

2.3.1.1. Inotropic Agents

Digoxin, a drug that exerts a direct inotropic effect on the heart, has been a therapeutic mainstay in CHF for many years. Despite this, the DIG (Digitalis Investigation Group) trial found that there was no significant impact on mortality in patients treated with digoxin.[31] However, this study demonstrated that patients treated with digitalis required less hospitalisation for worsening heart failure. The newer inotropic agents have also failed to lower the mortality rate of CHF sufferers. The PROMISE (Prospective Randomised Milrinone Survival Evaluation) trial, for example, did not live up to its name. Indeed there was a 28% higher all-cause mortality in patients randomly treated with 40 mg/day of milrinone compared to the placebo group.[32]

2.3.1.2. Vasodilators

The first Veteran Administration Co-operative Vasodilator-Heart Failure Trial (V-HeFT I) was published in 1986. The report showed that the addition of the vasodilators hydralazine (300 mg/day) and isosorbide dinitrate (160 mg/day) to a digoxin and diuretic regime resulted in a reduction in mortality of 38% after 1 year, 25% after 2 years, and 28% over the entire follow-up period (a mean of 2.3 years).[33] In 1991, the V-HeFT II study (conducted by the same group) reported that the angiotensin-converting enzyme (ACE) inhibitor

enalapril was 18% better than the combination of the two direct vasodilators.[34] However, the hydralazine-isosorbide combination was associated with improved ventricular function and better oxygen consumption at peak exercise.

2.3.1.3. Calcium Channel Blockers

Calcium channel blockers have been associated with worsening heart failure and a rise in mortality,[35] with the exclusion of amlodipine. The PRAISE (Prospective Randomised Amlodipine Survival Evaluation) trial found that while amlodipine had no impact on mortality, it diminished the combined risk of non-fatal and fatal events by 31% in patients with non-ischaemic cardiomyopathy.[36]

2.3.1.4. Beta-Adrenoceptor Blockade

The sympathetic system is activated in patients with CHF. Another way of dealing with the adverse effects of neurohumoral activation is through beta-adrenoceptor blockage. Carvedilol, for example, is a non-selective beta-receptor antagonist that also blocks alpha-1 receptors and has antioxidant effects. In a recent trial carvedilol reduced mortality, 6–12 months after treatment, by 65% in patients with CHF.[37] An Australian trial also showed improvement in ejection fraction, cardiac mortality and morbidity in patients treated with carvedilol.[38]

2.3.1.5. Angiotensin-Converting Enzyme Inhibitors

There is now a large volume of work supporting the role of ACE inhibitors in heart failure and these agents have become a cornerstone of first-line therapy. Treatment with ACE inhibitors improves haemodynamic profiles as well as functional status, with benefits in exercise performance, dyspnea, fatigue and edema. The Survival and Ventricular Enlargement (SAVE) trial showed improvement in all-cause mortality and reduced cardiovascular morbidity in patients with asymptomatic LV dysfunction after MI, who were treated with captopril.[39] The SOLVD (Studies of Left Ventricular Dysfunction) trial showed that enalapril reduced the risk of death and hospitalisation for worsening failure compared to the placebo group.[40]

There are many other studies showing the efficacy of various ACE inhibitor drugs in heart failure as a consequence of MI. However, while most of these drugs delay progression of heart failure for a while and provide a solid bedrock of therapy, each of them has a significant incidence of complications. Despite best medical therapy, patients tend to worsen gradually as the ventricle dilates inexorably.

2.3.2. Surgical Therapy

Apart from first-line treatment with drug therapy, a number of surgical techniques have also been developed to treat heart failure. These include the following.

2.3.2.1. Left Ventricular Assist Devices

Occasionally, in patients with cardiomyopathy due to either idiopathic or reversible causes, ventricular assist devices may be used on a long-term basis until the patients recover.[41] Despite many favourable reports[42] use of these devices has been bedevilled by a high rate of bleeding, infection and haemolysis,[43] as well as thrombo-embolism.[44] They work reasonably well in the short and intermediate term to tide patients over until transplantation.[45] However, ventricular devices are expensive and cumbersome. Because of the financial constraints, these are usually reserved for young patients in NYHA class IV heart failure who are likely to undergo a heart transplant.

2.3.2.2. Cardiomyoplasty

Dynamic cardiomyoplasty was first performed in 1985, utilising the left latissimus dorsi on an intact neurovascular pedicle. The skeletal muscle was transformed to fatigue resistance by long-term electrical stimulation, utilising Pette's elegant finding in muscle physiology.[46]

Skeletal muscle transformed in this way was used experimentally in an attempt to augment cardiac function[47] and as an implantable extra-aortic balloon assist device.[48] Despite much enthusiasm for this technique, early experiences were marred by high mortality and morbidity rates.[49] A randomised study to demonstrate the efficacy of cardiomyoplasty was commenced quite late; by the time the study was completed the cardiomyostimulators had already been withdrawn from the market. However, the results of the randomised study showed that

DropBooks

patients with NYHA class III heart failure who underwent cardiomyoplasty received symptomatic benefit.[50] Unfortunately, the results of this study came too late to resurrect this procedure.

2.3.2.3. Mitral Valve Annuloplasty

Bolling and his colleagues from Ann Arbor, Michigan, have advocated an aggressive approach to patients with dilated cardiomyopathy and mitral regurgitation. They have shown good intermediate term results with mitral valve repair, usually in the form of a radical annuloplasty to reduce the size of the mitral annulus.[51] This works well only if the mechanism of de-compensation is moderate to severe mitral regurgitation.

The Cleveland Clinic heart failure group, headed by Dr McCarthy, has reported good results with the Alfieri-type edge-to-edge mitral valve repair, along with an annuloplasty, in patients with mitral insufficiency in the setting of a cardiomyopathy.[52]

2.3.2.4. Partial Left Ventriculectomy (Batista Procedure)

As discussed previously, Dr Randas Batista was one of the first cardiac surgeons to demonstrate the beneficial possibilities of ventricular volume reduction surgery. Batista, working in a relatively impoverished area of Brazil, designed a procedure to reduce the size of dilated ventricles by resecting a portion of the left ventricular myocardium between the papillary muscles. He also advocated an Alfieri-type mitral valve repair. In 1997, he reported good results using this combined procedure.[53] There has been a lot of interest in the procedure with McCarthy, from the Cleveland Clinic, performing a careful evaluation of its efficacy. His findings showed that, in spite of a significant early morbidity and mortality, patients who survived had significant improvement in haemodynamics and ventricular function in the short-term.[54] Unfortunately, most patients had recurrent dilatation, which steadily progressed either to death or transplantation.[55]

2.3.2.5. Left Ventricular Aneurysm Repair

Reconstruction of scarred left ventricles in the setting of large left ventricular aneurysms is being performed with increasing frequency. Left ventricular aneurysms may be large saccular thin-walled scars or small dyskinetic scarred segments. In either case there is usually underlying cardiac dilatation. Early repairs of left ventricular aneurysms were performed in a linear fashion,[56] producing distortion of an already abnormal ventricle and often marginal results.[57] The importance of maintaining a geometric shape similar to that of a ventricle was demonstrated by various groups and resulted in the development of endo-aneurysmorrhaphy.[58]

In 1989 Dor[59] showed that endo-ventricular patch repair had physiologic merit and Jatene[60] demonstrated the importance of reducing the size of the defect after aneurysm resection. Late haemodynamic results are also favourable when patch repair of remodelled ventricular segments is performed in association with coronary artery grafting.[61]

In 1992 Dor went further and advocated reconstruction of post-ischaemic akinetic ventricular dilatation.[62] This was based on the observation that full-thickness scarring is prone to a variety of unpleasant sequelae, such as calcification, dykinesis, Dressler syndrome, and progressive dilatation of the remaining ventricular cavity.[63] A modification of this technique has also been developed for treatment of refractory ischaemic ventricular tachycardia by endo-ventricular patch plasty.[64] More recently, McCarthy reported on a series of patients undergoing ‘cardiac reshaping’ (which is akin to the Jatene procedure or the Dor procedure, but without the patch) for ischaemic dilated cardiomyopathy. This produced excellent results.[65] Buckberg is currently co-ordinating an international trial called SAVE (Surgical Anterior Ventricular Infarct Exclusion) to evaluate the efficacy of excluding the dyskinetic infarcted anterior segment of hearts in these patients.[66] Finally I would add that, to date, my personal experience with geometric endo-ventricular repair[67] has been very satisfactory in repairing anterior and inferior left ventricular scars. This technique incorporates features of the Cooley and the Dor repair without using a purse-string suture, but utilising a measured pericardial patch.

Cardiac transplantation is the accepted gold standard treatment for selected patients with refractory heart failure. Despite a 10-year survival of 65–70%, a shortage of donors means that it is available only for a very small subset of patients.[68]

2.3.3. Other Ancillary Therapies

2.3.3.1. Pacing

Pacing may be required to treat patients with symptomatic bradyarrhythmias or loss of atrioventricular synchrony. These pacemakers should be dual chambered and rate responsive.[69]

Biventricular pacing is a promising new approach to re-synchronise cardiac contraction in patients with systolic heart failure and left bundle branch blocks.[70] This approach is the subject of many international trials.

In selected patients with a propensity for ventricular arrhythmias, intra-cardiac cardioverter-defibrillator devices may be implanted, reducing the risks of out-of-hospital cardiac arrests.[71]

2.3.3.2. Exercise Training

In the 1990s there were various groups that showed the efficacy of low-intensity exercise training in patients with CHF.[72] On the basis of this experience, some groups have shown improvement in muscle strength[73] and haemodynamics with resistance training.[74] Whatever the intensity or mode, there is enough body of evidence now suggesting the beneficial effects of exercise in heart failure,[75,76] that most heart failure groups and clinics have an integrated programme that includes some form of physical exercise in addition to the general rehabilitative measures as treatment in patients with CHF.

2.4. Constraining the Heart—Prevention of Further Cardiac Dilatation

While some of the procedures mentioned so far help to reduce the size of the dilating ventricles (apart from cardiomyoplasty) none of them actually prevent further dilatation of the heart. In CHF, the natural tendency is for the heart to gradually enlarge over time. Our interest, then, was in developing a technique for not only reducing but also containing the size of the ventricle. We therefore decided to study the concept of ventricular containment based on what we thought was the presumed mechanism behind cardiomyoplasty. Fortunately there were a couple of papers that supported our premise that the muscle in myoplasty acted as a girdle[77] and that stimulation of the muscle actually gave it a bit of tension that improved the constraint.[78] Furthermore, a contemporaneous study reported good results using a goretex sheet wrapped around a dilating heart.[79] Raman and Power, working at the Austin Hospital, Melbourne, Australia, showed that this procedure could be adapted to various stages of progressive ventricular dilatation in an animal model, and this was adapted in human patients with encouraging results.[80] This proved the basis for various devices such as the Acorn cardiac support device, the Paracor device, etc, which will be discussed in Chapter 13.

Key Points to Remember

- Contestive heart failure is a complex clinical syndrome due to failure of the heart to meet the metabolic demands of the body.
- A variety of mechanisms get triggered initially from compensatory mechanisms in the cells of the heart.
- Over a period of time, these mechanisms take a life of their own to cause the various manifestations of heart failure.
- The clinical spectrum of heart failure is variable but is based on the underlying cellular, molecular mechanisms and end up causing a range of clinical manifestations.

DropBooks

References

1. Thomas L. The artificial heart. In: *Late Night Thoughts on Listening to Mahler's Ninth Symphony*. Viking Penguin, New York; 1983.
2. Willerson JT, Delgado R III, Mann D. Treating relentlessly progressive congestive heart failure: What next? *Tex Heart Inst J*. 1998;25:235-237.
3. Gheorghiade M, Bonow RO. Chronic heart failure in the United States: A manifestation of coronary artery disease. *Circulation*. 1998;97:282-289.
4. Willerson JT. Other cardiomyopathies. In: Willerson JT, Cohn JN eds. *Cardiovascular Medicine*. New York: Churchill Livingstone; 1995:888-894.
5. Luppi P, Rudert WA, Zanone MM, Stassi G, Finegold D, et al. Idiopathic dilated cardiomyopathy: A superantigen driven autoimmune disease. *Circulation*. 1998;98:777-785.

6. Cohn JN. Overview of pathophysiology of clinical heart failure. In: Hosenpud JD, Greenberg BH eds. *Congestive Heart Failure: Pathophysiology, Diagnosis and Comprehensive Approach to Management*. New York: Springer-Verlag; 1994:11-16.
7. Katz AM. The cardiomyopathy of overload: An unnatural growth response in the hypertrophied heart. *Ann Intern Med*. 1994;121:363-371.
8. McKay RG, Pfeffer MA, Pasternak RC, et al. Left ventricular remodelling after myocardial infarction: A corollary to infarct expansion. *Circulation*. 1986;74:693-702.
9. Torre-Amione G, Kapadia S, Benedict C, Oral H, Young JB, Mann DL. Pro-inflammatory cytokine levels in patients with depressed left ventricular ejection fraction: A report from the Studies of Left Ventricular Dysfunction (SOLVD). *J Am Coll Cardiol*. 1996;27:1201-1206.
10. Haywood GA, Tsao PS, von der Leyden HE, et al. Expression of inducible nitric oxide synthase in human heart failure. *Circulation*. 1996;93:1087-1094.
11. Oral J, Kapadia S, Nakano M, et al. Tumour necrosis factor-alpha and the failing human heart. *Clin Cardiol*. 1995;18(suppl 4):IV20-IV27.
12. Li G, Willerson JT. Molecular biologic alterations in heart failure. In: Frazier OH ed. *Support and Replacement of the Failing Heart*. Philadelphia: Linppincott-Raven; 1996:69-74.
13. Anversa P, Kajstura J, Olivetti M. Myocyte death in heart failure. *Curr Opin Cardiol*. 1996;11:245-251.
14. Hosenpud JD, Greenberg BH, eds. *Congestive Heart Failure: Pathophysiology, Diagnosis and Comprehensive Approach to Management*. New York: Springer-Verlag; 1994:623-624.
15. Bonow RO, Udelson JE. Left ventricular diastolic dysfunction as a cause of congestive heart failure: Mechanisms and management. *Ann Intern Med*. 1992;117:502-510.
16. Vasan RS, Benjamin EJ, Levy D. Prevalence, clinical features and prognosis of diastolic heart failure: An epidemiologic perspective. *J Am Coll Cardiol*. 1995;26:1565-1574.
17. Willerson JT, Cohn JN, eds. *Cardiovascular Medicine*. New York: Churchill-Livingstone; 1995:952–953.
18. Benedict CR. Neurohumoral aspects of heart failure. *Cardiol Clin*. 1994;12:9-23.
19. Hosenpud JD, Greenberg BH, eds. *Congestive Heart Failure: Pathophysiology, Diagnosis and Comprehensive Approach to Management*. New York: Springer-Verlag; 1994:13-14.
20. Cohn JN, Levine TB, Olivari MT, et al. Plasma norepinephrine as a guide to prognosis in patients with chronic congestive heart failure. *N Engl J Med*. 1984;311:819-823.
21. Meredith IT, Eisenhofer G, Lambert GW, Dewar EM, Jennings GL, Esler M. Cardiac sympathetic nervous activity in congestive heart failure: Evidence for increased neuronal norepinephrine release and preserved neuronal uptake. *Circulation*. 1993;88:136-145.
22. Wei CM, Lerman A, Rodeheffer RJ, et al. Endothelin in human congestive heart failure. *Circulation*. 1994;89:1580 -1586.
23. Mestroni L, Giacca M. Molecular genetics of dilated cardiomyopathy. *Curr Opin Cardiol*. 1997;12: 203-209.
24. Towbin JA, Hejtmancik JF, Brink A, et al. X-linked dilated cardiomyopathy: Molecular genetic evidence of the Duchenne muscular dystrophy (dystrophin) gene at Xp21 locus. *Circulation*. 1993;87:1854-1865.
25. Cintron G, Bigas C, Linares E, Aranda JM, Hernandez E. Nurse practitioner role in a chronic congestive heart failure clinic. In hospital time, costs and past satisfaction. *Heart Lung*. 1983;12:237-240.
26. Rich MW, Beckman V, Wittenber C, Level CL, Freedland KE, Carney RM. A multidisciplinary intervention to prevent the readmission of elderly patients with congestive heart failure. *N Engl J Med*. 1995;33:1190-1195.
27. Smith LE, Fabri SA, Pai R, Ferry D, Heywood T. Symptomatic improvement and reduced hospitalization for patients attending a cardiomyopathy clinic. *Clin Cardiol*. 1997;20:949-954.
28. Shepherd J, Cobbe SM, Ford I, et al., for the West of Scotland Coronary Prevention Study Group. Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *N Engl J Med*. 1995;333:1301-1307.
29. Scandinavian Simvastatin Survival Study Group. Randomized trial of cholesterol lowering in 4,444 patients with coronary heart disease: The Scandinavian Simvastatin Survival Study(4S). *Lancet*. 1994;344:1382-1389.
30. Squires RW, Lavie CJ, Brandt TR, Gau GT, Bailey KR. Cardiac rehabilitation in patients with severe left ventricular dysfunction. *Mayo Clin Proc*. 1987;62:997-1002.
31. Digitalis Investigation Group. The effect of digoxin on mortality and morbidity in patients with heart failure. *N Engl J Med*. 1997;336:523-533.
32. Packer M, Carver JR, Rodeheffer RJ, et al. for the PROMISE Study Research Group. Effect of oral milrinone on mortality in severe chronic heart failure. *N Engl J Med*. 1991;325:1468-1475.
33. Cohn JN, Archibald DG, Ziesche S, et al. Effect of vasodilator therapy on mortality in chronic congestive heart failure: Results of a Veterans' Administration Co-operative Study. *N Engl J Med*. 1986;314: 1547-1552.

34. Cohn JN, Johnson G, Ziesche S, et al. A comparison of enalapril with hydralazine-isosorbide nitrate in the treatment of chronic congestive heart failure. *N Engl J Med*. 1991;325:303-310.
35. The Multi-center Diltiazem Post-infarction Research Group. The effect of diltiazem on mortality and re-infarction after myocardial infarction. *N Engl J Med*. 1988;319:385-392.
36. Packer M, O'Connor CM, Ghali JK, et al., for the Prospective Randomized Amlodipine Survival Evaluation Study. Effect of Amlodipine on morbidity and mortality in severe chronic heart failure. *N Engl J Med*. 1996;335:1107-1114.
37. Packer M, Bristow MR, Cohn JN, et al., for the U.S. Carvedilol Heart Failure Study Group. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. *N Eng J Med*. 1996;334:1349 -1355.
38. Australia/New Zealand Heart Failure Research Collaborative Group. Randomized, placebo-controlled trial of carvedilol in patients with congestive heart failure due to ischaemic heart disease. *Lancet*. 1997;349:375-380.
39. Pfeffer MA, Braunwald E, Moye LA, et al, on behalf of the SAVE Investigators. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction: Results of the Survival and Ventricular Enlargement Trial. *N Engl J Med*. 1992;327:669 -677.
40. The SOLVD Investigators. Effect of enalapril on mortality and the development of heart failure in asymptomatic patients with reduced left ventricular ejection fractions. *N Engl J Med*. 1992;327:685-691.
41. Westaby S, Coats AFS. Mechanical bridge to recovery. *Eur Heart J*. 1998;19:541-547.
42. Schmid C, Hammel D, Deng MC, et al. Ambulatory care of patients with left ventricular assist devices. *Circulation*. 1999;100(suppl. II):II-224-II-228.
43. Mueller J, Wallukut G, Weng YG, et al. Weaning from mechanical cardiac support in patients with idiopathic dilated cardiomyopathy. *Circulation*. 1997;95:542-549.
44. Schmid C, Weyand M, Hammel D, Deng MC, Nabavi D, Scheld HH. Cerebral and systemic embolization during left ventricular support with the Novacor N100 device. *Ann Thorac Surg*. 1998;65:1703-1710.
45. Levin H, Chen J, Oz M, et al. Potential for left ventricular assist devices as outpatient therapy with awaiting transplantation. *Ann Thorac Surg*. 1994;58:1515-1520.
46. Pette D, Smith ME, Staudte HW, et al. Effects of long-term electrical stimulation on some contractile and metabolic characteristics of fast rabbit muscles. *Pfluegers Arch*. 1973;338:257-261.
47. Chachques JC, Grandjean PA, Carpentier A. Dynamic cardiomyoplasty: Experimental cardiac wall replacement with a stimulated skeletal muscle. In: Chiu RC-J ed. *Bio-mechanical Cardiac Assist: Cardiomyoplasty and Muscle-Powered Devices*. Mt Kisco, NY: Futura Publsishin Co; 1986:59-84.
48. Chiu RC-J, Walsh GL, Dewar ML, et al. Implantable extra-aortic balloon assist powered by transformed fatigue-resistant skeletal muscle. *J Thorac Cardiovasc Surg*. 1987;94:694-698.
49. Magovern JA, Furnary AP, Christlieb IY, Kao RL, Park SB, Magovern GJ. Indications and risk analysis for clinical cardiomyoplasty. *Seminars in Thoracic & Cardiovascular Surgery*. 1991;3(2):145-148.
50. Young JB, Kirklin JB. Cardiomyoplasty-Skeletal Muscle Assist Randomized Trial (C-SMART): 6 month results. *Circulation*. 1999;100[18(suppl. I)]:514.
51. Bolling SF, Deeb GM, Brunsting LA, et al. Early outcome of mitral valve reconstruction in patients with end-stage cardiomyopathy. *J Thorac Cardiovasc Surg*. 1995;104:676-683.
52. Bishay ES, McCarthy PM, Cosgrove DM, et al. Mitral valve surgery in patients with severe left ventricular dysfunction. *Eur J Cardiothorac Surg*. 2000;17:213-221.
53. Batista RJV, Nery P, Bocchino L, et al. Partial left ventriculectomy to treat end stage heart disease. *Ann Thorac Surg*. 1997;64:634-638.
54. Dowling RD, Koenig SC, Ewert DL, Cerrito P, Laureao MA, Gray LA. Does partial left ventriculectomy improve left ventricular systolic and diastolic function? *Circulation*. 1999;100[18(suppl. 1)]:801.
55. Starling RC, McCarthy PM, Hoercher KJ, Buda T, Goormastic M, Young JB. Partial left ventriculectomy for dilated cardiomyopathy: A viable option for end-stage heart failure? *Circulation*. 1999;100[18(suppl. 1)]:801.
56. Reddy SB, Cooley DA, Duncan JM, et al. Left ventricular aneurysm : Twenty-year surgical experience with 1572 patients at the Texas Heart Institute. *Cardiovasc Dis Bull Tex Heart Inst*. 1981;11:165-186.
57. Kesler KA, Fiore AC, Naunheim KS. Anterior wall ventricular aneurysm repair: A comparison of linear versus circular closure. *J Thorac Cardiovasc Surg*. 1992;103:841-848.
58. Jatene AD. Surgical treatment of left ventricular aneurysm. In: Baue AE, Geha AS, Hammond GL, Laks H, Naunheim KS eds. *Glenns's Thoracic & Cardiovascular Surgery*. Vol. 2. 5th ed. Norwalk, CT: Appleton & Lange; 1991:1829-1836.
59. DiDonato M, Dor V, Sabatier M, et al. Outcome of left ventricular aneurysmectomy with patch repair in

DropBooks

patients with severely depressed pump function. *Am J Cardiol*. 1995;76:557-561.
60. Cox JL. Surgical management of left ventricular aneurysms by the Jatene technique. In: Cox JL, Sundt TL, eds. *Operative Techniques in Cardiac & Thoracic Surgery—A Comparative Atlas*. Vol. 2. WB Saunders, Elsevier Publishing, Orlando FL; 1997:132-138.
61. Dor V. Sabatier M, DiDonato M, et al. Late hemodynamic results after left ventricular patch repair associated with coronary grafting in patients with post-infarction akinetic or dyskinetic aneurysm of the left ventricle. *J Thorac Cardiovasc Surg*. 1995;110:1291-1301.
62. Dor V. Reconstructive left ventricular surgery for post-ischemic akinetic dilatation. *Semin Thorac Cardiovasc Surg*. 1997;9(2):139-145.
63. Klein M, Herman M, Gorlin R. A hemodynamic study of left ventricular aneurysms. *Circulation*. 1967;35:614-630.
64. Dor V. The treatment of refractory ischemic ventricular tachycardia by endo-ventricular patch plasty reconstruction of the left ventricle. *Semin Thorac Cardiovasc Surg*. 1997;9(2):146-155.
65. Judd RM, Kim RJ, Chen E-L, et al. Contrast enhanced magnetic resonance imaging defines the pre-operative location and extent of myocardial scar prior to the Dor procedure. *Circulation*. 1999;100[18(suppl. 1)]:798.
66. Buckberg GD. Defining the relationship between akinesia and dyskinesia and the cause of left ventricular failure after anterior infarction and reversal of remodelling to restoration. *J Thorac Cardiovasc Surg*. 1998;116:47-49.
67. Raman J, Dixit A, Storer M, Hare DL, Buxton BF. Geometric endo-ventricular patch repair of inferior left ventricular scars improves mitral regurgitation and clinical outcome. *Ann Thorac Surg*. 2001;72:1055-1058.
68. Dabol R, Edwards NM. Cardiac transplantation and other therapeutic options in the treatment of end-stage heart disease. *Compr Ther*. 2000;26: 109-113.
69. Krum H, on behalf of the National Heart Foundation of Australia Chronic Heart Failure Clinical Practice Guidelines Writing Panel. Guidelines for management of patients with chronic heart failure in Australia. *Med J Aust*. 2001;174:459-466.
70. Barold SS. Biventricular cardiac pacing: Promising new therapy for congestive heart failure. *Chest*. 2000;118:1812-1819.
71. Hauer RN, Aliot E, Block M, et al. Indications for implantable cardioverter-defibrillator (ICD) therapy. Study Group on Guidelines on ICDs of the Working Group on arrhythmias of European society of cardiology. *Eur Heart J*. 2001;22:1074-1081.
72. Adamopoulos S, Coats A, Brunotte F, et al. Physical training imprives skeletal muscle metabolism in chronic heart failure. *J Am Coll Cardiol*. 1993;21:1101-1106.
73. Hare DL, Ryan TM, Selig SE, Pellizzer A, Wrigley TV, Krum H. Resistance exercise training increases muscle strength, endurance and blood flow in patients with chronic heart failure. *Am J Cardiol*. 1999;83:1674-1677.
74. McKelvie RS, Mccartney N, Tomlinson C, Baier R, MacDougall JD. Comparison of hemodynamic responses to cycling and resistance exercise in congestive heart failure secondary to ischemic cardiomyopathy. *Am J Cardiol*. 1995;76:977-979.
75. Honig B, Maier V, Drexler H. Physical training improves endothelial function in patients with chronic heart failure. *Circulation*. 1996;93:210-214.
76. Katz SD, Yuen J, Bijou R, LeJemtel TH. Training improves endothelium-dependent vasodilatation in resistance vessels of patients with heart failure. *J Appl Physiol*. 1997;82:1488-1492.
77. Copuya ER, Gerber RS, Drinkwater DJ, et al. Girdling effects of non-stimulated cardiomyoplasty on left ventricular function. *Ann Thorac Surg* 1993;56:867-870.
78. Patel HJ, Polidori DJ, Pila JJ, et al. Stabilisation of chronic remodelling by asynchronous cardiomyoplasty in dilated cardiomyopathy: Effects of a conditioned muscle wrap. *Circulation*. 1997;96:3665-3671.
79. Vaynbalt M, Chiavarelli M, Shah HR, et al. Cardiac binding in experimental heart failure. *Ann Thorac Surg*. 1997;64:81-85.
80. Raman J, Power JM, Buxton BF. Ventricular containment as an adjunct to conventional cardiac surgery. *Ann Thorac Surg*. 2000;70:1124–1126.

3
Strategies in Surgical Management

Irving L. Kron, R. Ramesh Singh, James D. Bergin, and Benjamin B. Peeler

The heart…moves of itself and does not stop unless for ever.

Leonardo da Vinci (1452–1519)

3.1. Introduction

Heart failure is not a disease but a complex clinical syndrome representing the end-stage of a number of different cardiac diseases. It can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill with or eject blood. It has been defined as a reduction in cardiac function such that cardiac output is reduced relative to the metabolic demands of the body and is associated with failure of compensating mechanisms.

Heart failure is one of the leading causes of hospitalization in the United States, with 400,000–700,000 new cases diagnosed yearly. Most current therapeutic strategies are focused toward resolving the acute exacerbation of failure, resulting in a 3-month readmission rate of 20% to 50% and a devastating 2-year mortality rate of 35–50%.[1,2] It currently affects more than five million people causing more than 700,000 deaths annually. Approximately a third of the heart failure patients are in New York Heart Association (NYHA) class III/IV (Table 3.1). The growing cost of caring for these patients approaches $50 billion per year.[3]

3.2. Pathophysiology

Heart failure can be categorized by specific mechanisms and manifestations. Two basic classifications are backward failure, first proposed in 1832 by Hope, and forward failure, suggested by Mackenzie about 80 years later. Backward failure refers to accumulation of blood upstream from the failing ventricle. This is represented by pulmonary edema in the face of left ventricular failure or systemic venous congestion in the setting of right-sided heart failure. Forward failure refers to the inadequacy of blood delivery into the pulmonary or systemic circulation due to the diminished pumping action of the right or left ventricle, respectively. Although these two hemodynamic states can be separated in theory, they almost invariably occur together. Both systolic and diastolic dysfunction contribute to the clinical picture. Systolic failure is more familiar and refers to pump failure, whereas diastolic failure is due to the impaired ability of the ventricle to fill properly. Heart failure most commonly refers to left-sided heart failure. Isolated right-sided heart failure can predominate but a mixed picture is usually typical in the clinical setting.[4]

3.3. Underlying Conditions

Underlying conditions that cause, exacerbate, or predispose to the development of heart failure should be identified and treated.

3.3.1. Ischemic Heart Disease

Coronary atherosclerosis is the commonest cause of cardiomyopathy in the United States, comprising 50–75% of patients with heart failure. In addition, coronary disease may be present in patients with heart failure of other causes, and may sometimes be overlooked as a contributing factor.[5] There are two mechanisms for heart failure in this setting: a prior myocardial infarction (MI) followed by left ventricular dysfunction and remodeling; or

DrugBooks

Table 3.1. New York Heart Association (NYHA) functional classification of cardiac disability.

I	Presence of cardiac disease but without limitations in physical activity. Normal physical activity does not cause fatigue, palpitation, dyspnea, or angina.
II	Presence of cardiac disease with mild limitation of physical activity. Comfortable at rest but normal physical activity causes fatigue, palpitation, dyspnea, or angina.
III	Presence of cardiac disease with marked limitation of physical activity. Comfortable at rest but less than normal physical activity causes fatigue, palpitation, dyspnea, or angina.
IV	Presence of cardiac disease with inability to perform any physical activity without discomfort. Discomfort even at rest with worsening of symptoms if activity is undertaken.

hibernating myocardium due to chronic but potentially reversible ischemic dysfunction. Patients with ischemic heart disease may have heart failure from one or both of these mechanisms.[6,7]

3.3.2. Valvular Heart Disease

Valvular heart disease is the primary cause of heart failure in perhaps 10–12% of patients.[8] Furthermore, valvular dysfunction is a secondary or superimposed phenomenon in many cases of heart failure. An example of this is that there is almost always some degree of mitral or tricuspid regurgitation in patients with severe dilated cardiomyopathy.[9]

Valvular dysfunction produces two forms of stress on the heart, volume overload and pressure overload. Both stresses result in increased cardiac afterload. Patients with valvular disease typically exhibit tremendous cardiac reserves. Because of the existence of various compensatory mechanisms, these patients can persist in an asymptomatic, well-compensated state until severe valvular and ventricular dysfunction has developed. In contrast, the patient developing acute valvular dysfunction without a period of gradual adaptation can rapidly succumb to severe heart failure.[4]

3.3.3. Other Factors

Other potentially reversible conditions that can impair ventricular function and cause, or worsen, heart failure should also be evaluated. This includes, but is not limited to, hypertension, renovascular disease, and drug therapy (a list of these drugs is shown in Table 3.2).[10]

3.4. Evaluation of Patients with Heart Failure

The approach to the patient with heart failure starts with the history and physical examination. Chest x-ray and a series of diagnostic tests are also used to establish the diagnosis, determine etiology, and assess acuity and severity. Recommendations for the evaluation of patients with heart failure were published in 2001 by an ACC/AHA Task Force and are shown in Table 3.3.[11]

As discussed previously, there are two major classes of symptoms in heart failure. First, backward failure leading to excess fluid accumulation, which results in dyspnea, edema, hepatic congestion, and ascites. Second, reduced cardiac output that is most pronounced with exertion, due to forward failure, causing fatigue and weakness.

3.4.1. Presenting Symptoms

The presenting symptoms are important in determining the acuity of heart failure. Acute and subacute presentations (days to weeks) are characterized primarily by dyspnea at rest and/or exertion. Other specialized forms of dyspnea, such as orthopnea and paroxysmal nocturnal dyspnea, are also common. Right heart failure and tachyarryhthmias may be present, resulting in symptomatology of hepatic congestion and palpitations, respectively.

Chronic presentations (months) differ in that fatigue, anorexia, bowel distention, and peripheral edema may be more pronounced than dyspnea. This is because pulmonary venous capacitance adapts to the chronic volume overload leading to less fluid accumulation in the alveoli, despite the increase in total lung water.

TABLE 3.2. Drugs associated with increased risk of adverse effects in patients with heart failure.

Drug class/Drug	Adverse effect(s)
Anti-inflammatory medications	
Corticosteroids	Sodium and fluid retention
Nonsteroidal anti-inflammatory drugs	Sodium and fluid retention; blunted response with diuretics; increased systemic vascular resistance
Cardiovascular medications	
Class I antiarrhythmic agents	Negative inotropy; proarrhythmia
Sotalol	Proarrhythmia
Ibutilide	Proarrhythmia
Minoxidil	Fluid retention; neurohumeral activation
Calcium channel blockers	Negative inotropy; neurohumeral activation
Diabetes medications	
Metformin	Lactic acidosis
Thiazolidinediones	Fluid retention
Hematologic medications	
Anagrelide	Phosphodiesterase inhibitor; palpiations; tachycardia; induction or exacerbation of heart failure
Cilostazol	Phosphodiesterase inhibitor; ventricular tachyarrthmias
Neurologic and psychiatric medications	
Amphetamines	Sympathetic agonist activity; hypertension; tachycardia;
Carbamazepine	Negative inotropic effect; bradyarrhythmias
Clozapine	Development of myocarditis and cardiomyopathy
Ergot alkaloids	Sympathetic agonist activity; valve fibrosis
Pergolide	Valve fibrosis
Tricyclic antidepressants	Negative inotropic effect; proarrhythmia
Miscellaneous	
Beta-2 agonists	Sympathetic agonist activity; tachyarrhythmias; hypokalemia

DropBooks

TABLE 3.3. Stages in the evolution of heart failure and recommended therapy by stage.[11]

Stage A	
At high risk for heart failure but without symptoms or structural heart disease	Treat hypertension Encourage smoking cessation Treat lipid disorders Encourage regular exercise Discourage alcohol intake or illicit drug use Angiotensin-converting enzyme inhibition in appropriate patients
Stage B	
Structural heart disease but without symptoms	Apply all measures used for Stage A Beta-blockers in appropriate patients
Stage C	
Structural heart disease with prior or current symptoms of heart failure	Apply all measures used in Stage A Drugs for routine use: Angiotensin-converting enzyme inhibitors Beta-blockers Digitalis Dietary salt restriction
Stage D	
Advanced heart disease and severe symptoms at rest despite maximal therapy. Refractory heart failure requiring specialized interventions	Apply all measures used in Stages A, B, and C Mechanical assist devices Heart transplantation Continuous intravenous inotropic infusions for palliation Hospice care

3.4.2. History

Although history alone is insufficient to make the diagnosis of heart failure,[12,13] it remains the single best discriminator to determine the acuity and rate of progression of heart failure. It also often provides important clues to the etiology of heart failure.

3.4.3. Physical Examination

Physical examination can provide important information concerning the degree of volume overload, ventricular enlargement, pulmonary hypertension, and reduced cardiac output.

3.4.4. Investigations

A standard workup should include blood tests, a chest x-ray, and electrocardiogram on all patients. The presence of pulmonary vascular congestion and cardiomegaly on chest x-ray support the diagnosis of heart failure. Chest x-ray is also useful for ruling out pulmonary disease in patients who present with dyspnea.[14–16] A normal electrocardiogram is unusual in patients with symptomatic systolic dysfunction (98% negative predictive value).[17]

Echocardiography should be performed on all patients with new onset of heart failure. It is one of the most useful noninvasive tools available in aiding the management of heart failure. In addition to having a high sensitivity and specificity for the diagnosis of heart failure (80% and 100%, respectively),[18] it can also detect other important findings. Regional wall motion assessment using dobutamine stress echocardiography may increase the ability to distinguish between ischemic and nonischemic dilated cardiomyopathy.[19] This technique is also useful in predicting recovery of cardiac function.[20,21] Echocardiography can also detect pericardial thickening, valvular heart disease, presence of thrombi, abnormal myocardial texture, chamber size and function, as well as measuring cardiac output using pulsed-wave Doppler.

Virtually all patients with unexplained heart failure should be evaluated for the presence of ischemic heart disease, as it is not an uncommon cause of dilated cardiomyopathy.[5,22] This can be done using several techniques.

Noninvasive exercise testing not only provides information about the existence of ischemic heart disease but can also be used for risk stratification and prognostic purposes. Measurement of the maximal oxygen uptake (VO_{2max}) provides an objective estimate of the functional severity of the myocardial dysfunction.

Coronary catheterization with angiography is indicated in patients with angina or a positive exercise stress test. However, even in patients with a normal exercise stress test, who otherwise have unexplained heart failure, cardiac catheterization should strongly be considered. The ACC/AHA Committee on Coronary Angiography has published recommendations for the use of coronary angiography in patients with heart failure as shown in Table 3.4.[23] It may also detect and grade the underlying valvular heart disease, which may contribute to the symptomatology of heart failure.

The role of endomyocardial biopsy in discovering the etiology of dilated cardiomyopathy is not well defined. The yield for clinically useful information not obtainable without biopsy is low.[22,24,25] Hence, it should be reserved for patients with suspected systemic diseases known to affect the myocardium, including hemochromatosis, amyloidosis, and sarcoidosis.

3.5. Current Management Strategies

Traditionally, heart failure has been thought to be secondary to impaired left ventricular function. This would imply that contractile failure causes systolic dysfunction. However, it is currently thought that systolic dysfunction is secondary to a structural increase in ventricular chamber volume. Hence, instead of chamber dilatation occurring as a result of contractile failure, it happens as an early response to reduced wall motion, which is necessary to generate a normal stroke volume from a larger end-diastolic volume. As a result, alterations in chamber length and shape, which are not related to a preload-mandated increase in sarcomere length, occur. This pathologic change is termed remodeling. As the heart remodels and dilates, the radius of curvature increases. According to LaPlace's law, this results in greater wall tension that increases myocardial oxygen

TABLE 3.4. Recommendations for use of coronary angiography in patients with heart failure (HF).

Class I
1. HF due to systolic dysfunction with angina or with regional wall motion abnormalities and/or scintigraphic evidence or reversible myocardial ischemia when revascularization is being considered.
2. Before cardiac transplantation.
3. HF secondary to postinfarction ventricular aneurysm or other mechanical complications of myocardial infarction (MI).

Class IIa
1. Systolic dysfunction with unexplained cause despite noninvasive testing.
2. Normal systolic function, but episodic heart failure raises suspicion of ischemically mediated left ventricular dysfunction.

Class III
1. HF with previous coronary angiograms showing normal coronary arteries, with no new evidence to suggest ischemic heart disease.

ACC/AHA classification

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.
Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment
Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
Class IIb: Usefulness/efficacy less well established by evidence/opinion.
Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful and in some cases may be harmful.

consumption, decreases subendocardial blood flow, impairs energetics, and increases arrhythmias. Overall, the degree of remodeling correlates directly with poor prognosis.[26] According to this view, remodeling, not contractile failure, is the key to the severity of reduced ejection fraction and poor prognosis. Fortunately, some aspects of the remodeling process have been shown to be reversible.[27–32]

Tremendous progress has been made over the past 20 years in the management of heart failure. For many years, medical management has remained the mainstay of therapy. Current pharmacological therapies that improve mortality can inhibit progressive chamber remodeling and improve survival. A number of drugs are commonly used in heart failure for symptom relief and improvement of outcome. There have been several large trials that demonstrated improved mortality, left ventricular function, long-term outcomes, and decreased hospitalization rate with the administration of angiotensin-converting enzyme (ACE) inhibitors[33–35] and new generation beta-blockers.[36–40] Further data suggest that the survival benefits can be attributed to the reversed remodeling properties of these drug groups.[41–43]

Nevertheless, despite significant advances in the pharmacological support of the failing heart, the results are far from perfect. Mortality remains high and hospitalization costly. Surgical management is still required for patients with end-stage heart failure. Unfortunately, its evolution has occurred in a less structured fashion. Heart transplantation remains the treatment of choice for many patients with end-stage heart failure who remain symptomatic despite optimal medical therapy. Similar to other forms of transplantation, the persistent shortage of donor hearts and strict selection criteria continue to limit the annual growth of this approach. Thus, heart transplantation is not an available option for most patients with heart failure and continues to be performed only at large, highly specialized medical centers.

3.6. Surgical Management of Heart Failure

Surgical techniques employed for end-stage heart failure are under active investigation. Although large randomized multicenter trials are unusual in this field, important progress is being

made. Specialized strategies considered include implantation of pacemakers, coronary revascularization, left ventricular reconstruction, mitral valve repair, cardiomyoplasty, and mechanical circulatory support.

3.6.1. Pacemaker Implantation

General indications for pacemaker implantation include patients with chronic atrial fibrillation who require atrioventricular nodal ablation for rate control and symptomatic bradycardias. The use of biventricular (BiV) pacemakers, termed resynchronization therapy, can improve symptoms in some patients with moderate to severe heart failure.[44,45] As a result of this, BiV pacing has been approved by the USFDA as a treatment for moderate to severe heart failure. However, it has not determined when BiV pacing should be used. This is due to potential concerns, which include a small risk of serious complications occurring during implantation[44] and a lack of long-term data.[11] It is also not known if these devices should routinely be used with an implantable defibrillator.

3.6.2. Left Ventricular Reconstruction

In heart failure, both ventricular enlargement, resulting from damaged myocardium, and a ventricular aneurysm, which can develop after a heart attack, can compromise the heart's ability to produce a strong contraction and leads to a decrease in cardiac output. Batista et al. first introduced the concept of surgically reversing this process, partial left ventriculectomy, for patients with NYHA class IV idiopathic dilated cardiomyopathies in 1996. They described a procedure that involved resection of normal muscle between both papillary muscles and extending from the apex to the mitral annulus. The mitral valve was either preserved, repaired, or replaced depending on the amount of tissue removed. This restored the ventricle to a more normal volume/mass/diameter relationship.[46] The reduction in ventricular diameter, according to LaPlace's law, results in decreased ventricular wall tension and possibly a more uniform pattern of contraction/relaxation, thus improving systolic performance.[47,48] Although many patients initially improved markedly,[47,49–55] the perioperative mortality was high and many patients redilated[49,56] with a high recurrence rate of symptomatic heart failure.[51,55,57] As a consequence, overall enthusiasm for the procedure has waned.

The newer surgical modalities for cardiomyopathy have benefited from the lessons learned in the treatment of left ventricular aneurysms. The Dor procedure is an approach to surgical reconstruction in the setting of postinfarction aneurysm formation.[58] Prior to the development of the Dor procedure, surgical treatment for postinfarction aneurysms involved removal of the aneurysmal area and reapproximation of the viable wall (endoaneurysmorraphy) in an attempt to restore left ventricular geometry. However, this approach has not been found to improve left ventricular performance.[59] In the Dor procedure, also called endoventricular circular patch plasty (EVCPP), a purse-string stitch is placed around the circumference of the nonviable scarred aneurysm to minimize the excluded area. The size of the scar is more important than whether it is akinetic or dyskinetic. Larger scars may yield a greater improvement in left ventricular ejection fraction (LVEF) but have a significantly higher perioperative mortality rate (12% versus 2.2% for a small scar). The residual defect is then covered with a Dacron, pericardium, or an autologous tissue flap. This operation shortens the long axis, leaving the short axis length unchanged, producing an increase in ventricular diastolic sphericity while the systolic shape becomes more elliptical.[60,61] This results in a more normal geometry and improved systolic performance. The overall operative mortality in the first patients who underwent the Dor procedure was 8%. Operative mortality was higher when surgical repair was performed urgently 16.3% compared to 6.2% when it was planned.[62] The overall improvement in LVEF was maintained at 1 year. Also, there was a reduction in the end-diastolic volume index and symptomatic heart failure status improved by 92%.[63]

A modification of the Dor procedure, surgical anterior ventricular endocardial restoration (SAVER), consists of exclusion of noncontracting segments in the dilated remodeled ventricle after an anterior MI. The efficacy of this approach was evaluated in the multicenter RESTORE trial; 89% also underwent bypass grafting and 26% had mitral valve repair or replacement. It revealed a significant reduction in left ventricular end-systolic volume index and an increase in LVEF from 29% to

39%.[62] Furthermore, it has been noted that the Dor procedure ameliorates mitral regurgitation (MR) in a majority of cases even in the absence of associated mitral valve procedures, probably due to the reduction in the size of the ventricle and improved orientation of the papillary muscles.[64] The choice of the beating-heart approach or continuous aortic cross-clamp plays little to no role in postoperative outcome. Furthermore, the added ischemic time associated with continuous cross-clamp is outweighed by the potential benefits.[65] Cope et al. conducted a cost comparison of heart transplantation versus alternative operations for cardiomyopathy in 2001.[66] This study compared the cost and survival among patients who have undergone heart transplantation, isolated coronary artery bypass grafting (CABG), mitral valve replacement, and the Dor procedure. It was noted that the total cost of heart transplantation, which included the procurement costs, was significantly higher. The cost was comparable among the other three groups. The operative survival was similar among the four groups. Thus, ventricular reconstructive surgery is a practical alternative to heart transplantation in select patients. Recommendations for the indications for ventricular reconstructive surgery have been proposed in a 2002 review as shown in Table 3.5.[63]

3.6.3. Mitral Valve Repair

Mitral regurgitation (MR) is often a complication of end-stage cardiomyopathy. It can result from dilatation of the mitral annular-ventricular apparatus with altered geometry and ischemic papillary muscle dysfunction.[67,68] Although the teaching for decades has been that closing off the mitral valve leak removes the "pop-off" valve and is associated with an unacceptable surgical death rate, it is important to keep in mind that the regurgitation of blood into the left atrium leads to a cycle of more volume overload, which can lead to progressive annular dilatation, worsened MR, and more severe symptoms of congestive heart failure.[69] Severe MR in patients with ischemic cardiomyopathy is a difficult management issue. Not only do these patients have worsened symptoms, but they also have an increased death rate. The reported 1-year survival rate for medical therapy in this subset of patients is less than 20%.[70] Among patients with significant (>2+) secondary MR, mitral valve repair should be considered in NYHA class III/IV patients with dilated cardiomyopathies.[3] Several studies have shown that mitral valve repair in patients with end-stage cardiomyopathy is not only feasible but also improves ventricular function and overall survival.[70–75] If mitral valve repair is not possible, it is essential that mitral valve replacement be performed with retention of the subchordal attachments. Preservation of both the anterior and posterior chorded attachments to the papillary muscles helps to maintain normal ventricular geometry and function following mitral valve replacement.[76–79] Most of these studies, however, have dealt with mitral valve repairs in patients with nonischemic dilated cardiomyopathy.

Ischemic MR seems to be more complex. Often the posterior leaflet becomes functionally restricted owing to ventricular enlargement. Patients with severe MR secondary to ischemic cardiomyopathy have two separate pathophysiologies that not only augment pump failure but also need to be each dealt with separately surgically. The surgical management of these patients, particularly those requiring both mitral valve surgery and concomitant CABG, has traditionally been associated with an increased surgical risk.[80] Clearly these patients represent a substantial increased surgical risk compared with patients undergoing either CABG or mitral valve surgery alone.[72] Fortunately, with the advances in myocardial protection and surgical techniques, some of these more difficult patients are now not only at a lower surgical risk but also are experiencing improvements in their symptomatic status. A more recent study concluded that concomitant CABG and mitral valve repair compare favorably

TABLE 3.5. Indications for ventricular reconstructive surgery.

1. Anteroseptal myocardial infarction (MI), with dilated left ventricle (end-diastolic volume index > 100 ml/m^2), and
2. Depressed left ventricular ejection fraction (LVEF) (even under 20%), and
3. Left ventricular regional dyskinesis or akinesis of greater than 30% of the ventricular perimeter, and
4. At least one of the following:
   a) symptoms of heart failure
   b) arrhythmias
   c) ischemia on provocative tests in asymptomatic patients

DropBooks

to both CABG alone and cardiac transplantation, thus offering a reasonable alternative for this patient population.[81]

3.6.4. Surgical Revascularization

Heart failure resulting from coronary artery disease (CAD) is usually due to MI and subsequent ventricular remodeling. When the ischemia is chronic, the recoverable or viable myocardium is termed "hibernating" but when the insult is transient that myocardium is described as "stunned." The impaired left ventricular function in these patients is not entirely an irreversible process, if hibernating myocardium is in part responsible to the decline in myocardial function. About 40% of segments involved in MI may subsequently recover, either spontaneously or after revascularization. Also, LVEF may improve markedly, and even normalize, in subsets of patients following successful revascularization.[82,83] Patients with documented viability by thallium perfusion imaging, PET scanning, or dobutamine echocardiography had significant 80% reduction in annual mortality with revascularization. There was a direct relationship between severity of left ventricular dysfunction and magnitude of benefit. In contrast, there was no difference in outcome with revascularization or medical therapy in patients without viability.[7]

Surgical revascularization for patients with ejection fractions of $<20\%$ to recruit hibernating myocardium is now becoming commonplace.[84] These patients are generally sicker with more preoperative risk factors. However, despite increased hospital mortality of about 4–6%, they enjoy 90% 1-year survival and 64% 5-year survival.[85] Patients with ischemic cardiomyopathy, evidenced by viable myocardium, and bypassable vessels can be revascularized with permissible risk, achieving 88% perioperative survival with 72% of patients alive at 1 year. These results are reproducible and have been reported by different authors.[86–89]

It is commonly believed that patients with both ischemic cardiomyopathy and significant left ventricular dilatation should undergo transplantation secondary to poor outcome after CABG.[90] However, Aziz and associates[91] addressed this issue by comparing the outcomes of cardiac transplantation between patients with ischemic cardiomyopathy and those with idiopathic cardiomyopathy. Although the operative mortality between the two groups was essentially the same (11.2% and 10.6%, respectively), the 10-year survival was remarkably different (39% and 80%, respectively). Hence, the decision to operate on patients with severely depressed left ventricular function is not straightforward. There are excellent short-term results with CABG alone but inferior midterm results compared with CABG plus ventricular remodeling.[92]

3.6.5. PTCA Versus CABG

The usefulness of angioplasty depends upon the pattern and extent of arterial narrowing. Angioplasty is often recommended over bypass surgery when arterial narrowing is mild or moderate and when only one or two coronary arteries are narrowed. It is more effective in patients who do not have diabetes mellitus. Patients with diabetes appear to have a greater benefit from CABG, especially in the setting of multivessel, multilesion, or severe CAD.[93]

Recommendations for revascularization for patients with native-vessel CAD by the ACC/AHA/ACP-ASIM are shown in Table 3.6.[94] These recommendations were ratified again in the 2002 update.

The randomized trials of initial medical treatment versus initial surgery showed that patients with left main stenosis greater than 69% and those with multivessel CAD with a proximal left anterior descending artery stenosis greater than 69% have a better late survival rate if they have coronary bypass surgery. Because the randomized trials of percutaneous transluminal coronary angioplasty (PTCA) versus bypass surgery included an inadequate number of patients in these high-risk subsets, it cannot be assumed that the alternative strategy of PTCA produces equivalent late survival in such patients.

Meta-analysis of the randomized trials of medical management versus CABG have further indicated that patients without severe symptoms but with a proximal left anterior descending artery lesion have a better survival rate with surgery, even if they have normal left ventricular function and only 1-vessel disease. For these patients, data from the PTCA versus CABG trials appear to show that, at least for the first 5 years, the alternative revascularization strategy of PTCA does not compromise survival for patients who are good angiographic candidates for PTCA.[94]

TABLE 3.6. Recommendations for revascularization with percutaneous transluminal coronary angioplasty (PTCA) and coronary artery bypass graft (CABG) in patients with stable angina.

Class I
1. CABG for patients with significant left main coronary disease.
2. CABG for patients with 3-vessel disease. The survival benefit is greater in patients with abnormal left ventricular (LV) function (ejection fraction < 50%).
3. CABG for patients with 2-vessel disease with significant proximal left anterior descending coronary artery disease (CAD) and either abnormal LV function (ejection fraction < 50%) or demonstrable ischemia on noninvasive testing.
4. PTCA for patients with 2- or 3-vessel disease with significant proximal left anterior descending CAD, who have anatomy suitable for catheter-based therapy, normal LV function, and who do not have treated diabetes.
5. PTCA or CABG for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD but with a large area of viable myocardium and high-risk criteria on noninvasive testing.
6. CABG for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD who have survived sudden cardiac death or sustained ventricular tachycardia.
7. In patients with prior PTCA, CABG, or PTCA for recurrent stenosis associated with a large area of viable myocardium and/or high-risk criteria on noninvasive testing.
8. PTCA or CABG for patients who have not been successfully treated by medical therapy and can undergo revascularization with acceptable risk.

Class IIa
1. Repeat CABG for patients with multiple saphenous vein graft stenoses, especially when there is significant stenosis of a graft supplying the left anterior descending coronary artery. PTCA may be appropriate for focal saphenous vein graft lesions or multiple stenoses in poor candidates for reoperative surgery.
2. PTCA or CABG for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD but with a moderate area of viable myocardium and demonstrable ischemia on noninvasive testing.
3. PTCA or CABG for patients with 1-vessel disease with significant proximal left anterior descending CAD.

Class IIb
1. Compared with CABG, PTCA for patients with 3- or 2-vessel disease with significant proximal left anterior descending CAD who have anatomy suitable for catheter-based therapy and who have treated diabetes or abnormal LV function.
2. PTCA for patients with significant left main coronary disease who are not candidates for CABG.
3. PTCA for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD who have survived sudden cardiac death or sustained ventricular tachycardia.

Class III
1. PTCA or CABG for patients with 1- or 2-vessel CAD without significant proximal left anterior descending CAD who have mild symptoms that are unlikely due to myocardial ischemia or have not received an adequate trial of medical therapy and
   a) Have only a small area of viable myocardium or
   b) Have no demonstrable ischemia on noninvasive testing.
2. PTCA or CABG for patients with borderline coronary stenoses (50–60% diameter in locations other than the left main) and no demonstrable ischemia on noninvasive testing.
3. PTCA or CABG for patients with insignificant coronary stenosis (<50% diameter).
4. PTCA in patients with significant left main CAD who are candidates for CABG.

Note: PTCA is used in these recommendations to indicate PTCA and/or other catheter-based techniques such as stents, atherectomy, and laser therapy.

ACC/AHA classification

Class I: Conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.
Class II: Conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment.
Class IIa: Weight of evidence/opinion is in favor of usefulness/efficacy.
Class IIb: Usefulness/efficacy less well established by evidence/opinion.
Class III: Conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful and in some cases may be harmful.

Reproduced with permission from Gibbons RJ, Chatterjee K, Daley J, et al.[94] Copyright © 2007 Elsevier B.V. All rights reserved.

DropBooks

3.6.6. Mechanical Circulatory Support

Circulatory assist devices were initially designed to support patients in hemodynamic collapse. Currently, they can be used in a wide range of clinical conditions including refractory heart failure. It is an established therapy as a bridge to transplantation with 70% of patients successfully transplanted after implantation of a left ventricular assist device.[3] These devices allow patients to be

sent home while awaiting a suitable donor heart. They also allow these patients to be mobile and rehabilitated prior to their transplantation.

Ventricular assist devices have many beneficial effects on myocardial function, which includes improvement in contractile performance, reversal of the downregulation of beta-receptors seen in heart failure, and normalization of chamber geometry with a reduction in myocardial fibrosis.[95–98]

These devices can be divided into four main categories.

3.6.6.1. Counterpulsation Devices (Intra-Aortic Balloon Pump)

This is the most commonly used mechanical support that has had a long record of success. It is simple in design, easy to use, and least expensive. This type of device is of limited use, however, in patients with significant peripheral vascular disease, those with aortic dissections, and those with significant aortic regurgitation.

3.6.6.2. Cardiopulmonary Assist Device

This has limited use outside the cardiac catheterization laboratory. It provides full cardiopulmonary support analogous to that provided by bypass during cardiac surgery.

3.6.6.3. Left Ventricular Assist Devices

These can be further divided into intermediate and long-term devices. The intermediate-term devices can be thought of as true bridges to transplantation. They are intended to be removed during transplantation and are not designed for chronic, permanent support.[99]

Long-term devices were designed as replacement therapy for patients with heart failure. Although they are FDA approved as a bridge to transplantation, patients with severe disease who are not eligible for transplantation have improved survival with long-term left ventricular assist devices compared to optimal medical therapy alone.[100]

3.6.6.4. Total Artificial Heart

Another type of mechanical device is the total artificial heart. It is inserted orthotopically accompanied by the removal of the patient's own ventricles. A study in 2004[101] found that patients supported with the total artificial heart, compared to controls, had a significantly higher rate of survival to transplantation (79% versus 46%) and of overall survival at 1 year (70% versus 31%). Complications, which include infection, thromboembolism, and bleeding, were frequent but deemed to have only affected the outcome in a minority of patients.

Mechanical devices with increased longevity are currently in trial or development. These may obviate the need for heart transplantation in the future for a significant number of patients.

3.6.7. Cardiomyoplasty

Dynamic cardiomyoplasty is a procedure in which skeletal muscles are taken from a patient's back or abdomen, wrapped around an ailing heart, and paced during ventricular systole. This procedure is experimental and performed only in limited numbers. Some studies have shown that in patients undergoing this procedure, the operative mortality decreased and there was an improvement in symptoms.[102] However, long-term outcome data with cardiomyoplasty are limited and its future for chronic heart failure remains uncertain.[103]

3.6.8. Mechanical Inhibition of Dilatation

The Acorn CorCap cardiac support device is a simple, yet profound, new investigational strategy for treating moderate heart failure. It is intended to be an adjunctive therapy with standard medical and surgical heart failure management for patients with dilated cardiomyopathy. The biocompatible, mesh-like jacket is drawn up and anchored around the ventricles. By supporting the heart and reducing stress-mediated myocardial stretch, left ventricular dilatation is limited with improvement in LVEF. Preliminary data suggest that the device produces an improvement in heart failure symptoms, LVEF, end-diastolic and end-systolic dimensions, and quality of life.[104]

3.6.9. Cardiac Transplantation

Cardiac transplantation is the treatment of choice for many patients with end-stage heart failure who remain symptomatic despite optimal

medical therapy. It can improve both survival and quality of life in this patient population. In 1999, the International Society for Heart and Lung Transplantation reported that there was annual mortality rate of approximately 4% after the first year of heart transplantation. The survival rate was 79% at 1 year and 50% at 8.8 years overall.[105]

Patients who should be considered for heart transplantation are listed in Table 3.7.[106] The main indications are to improve survival and to enhance the quality of life. This benefit is easy to demonstrate in the moribund, hospitalized patients, but is less clear in many ambulatory patients. In keeping with the recommendations from the ACC/AHA Task Force,[11] the minimum requirements for consideration for cardiac transplantation are as follows:

A history of repeated hospitalizations for heart failure

Escalation of intensity for medical therapy

A reproducible VO_{2max} of less than 14 ml/kg/min is a relative indication, while a VO_{2max} of less than 10 ml/kg/min is an absolute indication in otherwise appropriate candidates

Other indications recommended by the ACC/AHA Tack Force include the following:

Refractory cardiogenic shock

Continued dependence on intravenous inotropes to maintain adequate organ perfusion

Severe symptoms of ischemia that limit routine activity and are not amenable to revascularization (absolute indication) or recurrent unstable angina not amenable to other intervention (relative indication)

Severe symptomatic ventricular arrhythmias refractory to all therapies

3.7. Summary

To summarize, the surgical management for patients with heart failure can be divided into two broad categories based on the type of underlying cardiomyopathy. Hence, care must be taken to accurately diagnose these patients as either having dilated cardiomyopathy or ischemic cardiomyopathy. There are not many surgical options available for dilated cardiomyopathy. If maximal medical therapy, which includes BiV pacing for a widened QRS complex, has failed, these patients are usually referred for cardiac transplant evaluation. Mitral valve repair is performed in these patients, for MR of 2+ or greater, if they are appropriate surgical candidates. The role of the various cardiac wraps still remains unclear. Ventricular assist devices can be used here as a bridge to transplantation if the patient becomes unstable.

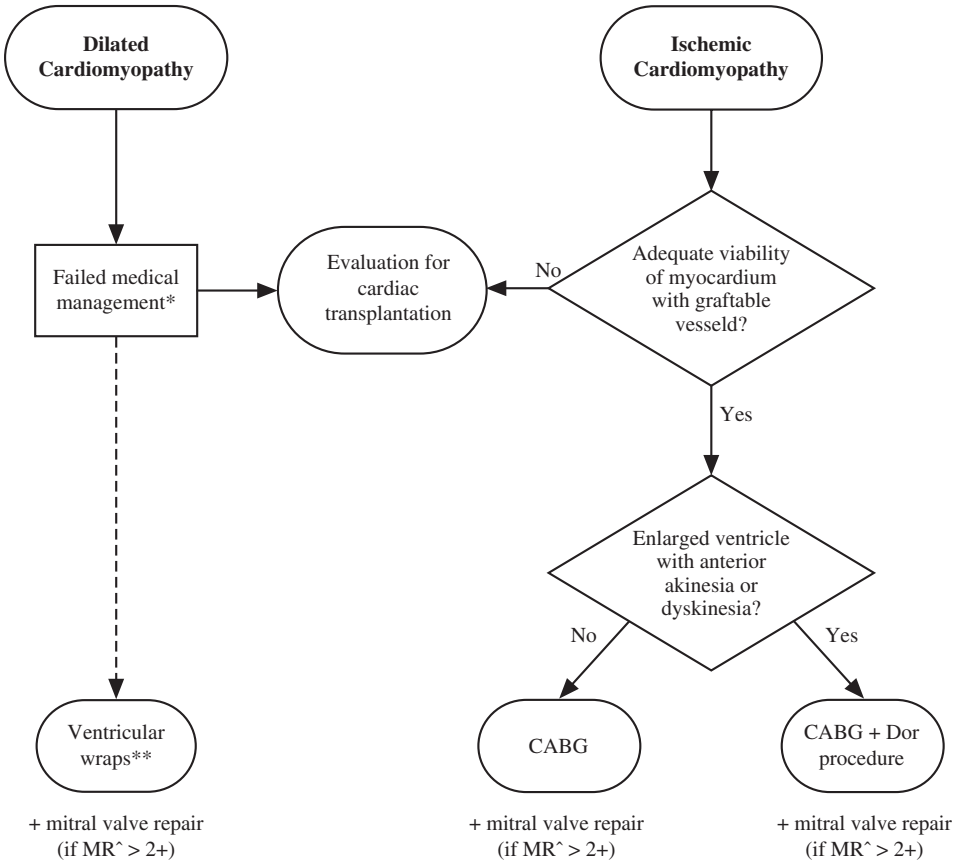
DropBooks

Table 3.7. Criteria for patients with heart disease considered for cardiac transplantation who do not respond to maximal medical therapy.[106]

A. Systolic heart failure as defined by left ventricular ejection fraction (LVEF) <35%
Excluded etiologies
1) Amyloid
2) Human immunodeficiency virus (HIV)
3) Cardiac sarcoma
B. Ischemic heart disease with intractable angina
1) Not amenable to coronary artery bypass graft (CABG) or percutaneous coronary intervention
2) Maximal tolerated medical therapy not effective
3) Rejected for direct myocardial revascularization or transmyocardial revascularization or the procedure attempted was unsuccessful
C. Intractable arrhythmia that is uncontrolled with implantable cardioverter-defibrilattor
1) Not amenable to electrophysiologic-guided single or combination medical therapy
2) Not a candidate for ablative therapy
D. Hypertrophic cardiomyopathy with NYHA class IV symptoms that persist despite maximal therapy
1) Alcohol injection
2) Myomectomy
3) Mitral valve replacement
4) Pacemaker therapy
E. Congenital heart disease in which fixed pulmonary hypertension is not a complication

The surgical management of heart failure due to ischemic cardiomyopathy is more complex. Treatment options depend on the size of the ventricles and the presence or absence of MR. As in patients with dilated cardiomyopathy, mitral valve repair is warranted for patients with MR of 2+ or greater. Patients with ischemic cardiomyopathy who have no valve pathology should have a CABG, if there is viable myocardium and graftable vessels. However, the Dor procedure should be performed concurrently with CABG if these patients also have enlarged ventricles with anterior akinesia or dyskinesia. Cardiac transplantation is reserved for failure of the above strategies or if there is insufficient viable myocardium (Figure 3.1).

Heart failure is a major cause of mortality and morbidity in the United States. Although medical treatment in improving, a substantially large



* Includes biventricular pacing in presence of widened QRS complex

* * Insufficient data presently to support this approach

^ Mitral regurgitation

Refer for cardiac transplant evaluation if failure of surgical strategy

FIGURE 3.1. Algorithm for surgical management of heart failure. The *asterisk* indicates that it includes biventricular pacing in presence of widened QRS complex. The *double asterisks* indicates insufficient data presently to support this approach. The *caret* indicates mitral regurgitation (MR). Refer for cardiac transplant evaluation if failure of surgical strategy.

proportion of patients with heart failure should be considered for more advanced therapies. An aggressive approach to surgical revascularization, correction of mitral insufficiency, or reversal of left ventricular remodeling should be considered in any patient who has exhausted pharmacologic therapy. Such procedures should be performed in large dedicated centers that have specialized expertise with these therapies in patients with end-stage heart failure.

Key Points to Remember

- Heart failure is a major cause of mortality and morbidity in the US, the developed world and the developing world.
- Patients are best evaluated by multi-disciplinary teams.
- Surgical therapy is offered for patients who fail medical management.
- Patients are typically evaluated for cardiac transplantation as definitive therapy for end-stage heart failure.
- Alternative therapies are recommended for a variety of conditions.

DropBooks

References

1. Mills RM, Young JB. *Practical Approaches to the Treatment of Heart Failure*. Baltimore, Philadelphia: Williams & Wilkins; 1998.
2. Carson PE. Beta blocker treatment in heart failure. *Prog Cardiovasc Dis*. 1999;41(4):301-321.
3. Zeltsman D, Acker MA. Surgical mana gement of heart failure: An overview. *Annu Rev Med*. 2002;53:383-391.
4. Greenfield LJ, Mulholland MW. *Surgery: Scientific Principles and Practice*. 2nd ed. Philadelphia: Lippincott-Raven Publishers; 1997.
5. Bortman G, Sellanes M, Odell DS, Ring WS, Olivari MT. Discrepancy between pre- and post-transplant diagnosis of end-stage dilated cardiomyopathy. *Am J Cardiol*. 1994;74(9):921-924.
6. Marwick TH. The viable myocardium: Epidemiology, detection, and clinical implications. *Lancet*. 1998;351(9105):815-819.
7. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: A meta-analysis. *J Am Coll Cardiol*. 2002;39(7):1151-1158.
8. Baldasseroni S, Opasich C, Gorini M, et al. Left bundle-branch block is associated with increased 1-year sudden and total mortality rate in 5517 outpatients with congestive heart failure: A report from the Italian network on congestive heart failure. *Am Heart J*. 2002;143(3):398-405.
9. Koelling TM, Aaronson KD, Cody RJ, Bach DS, Armstrong WF. Prognostic significance of mitral regurgitation and tricuspid regurgitation in patients with left ventricular systolic dysfunction. *Am Heart J*. 2002;144(3):524-529.
10. Amabile CM, Spencer AP. Keeping your patient with heart failure safe: A review of potentially dangerous medications. *Arch Intern Med*. 2004;164(7):709-720.
11. Hunt SA, Baker DW, Chin MH, et al. ACC/AHA guidelines for the evaluation and management of chronic heart failure in the adult: Executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to revise the 1995 Guidelines for the Evaluation and Management of Heart Failure). *J Am Coll Cardiol*. 2001;38(7):2101-2113.
12. Davie AP, Francis CM, Caruana L, Sutherland GR, McMurray JJ. Assessing diagnosis in heart failure: Which features are any use? *QJM*. 1997;90(5): 33-339.
13. Morgan S, Smith H, Simpson I, et al. Prevalence and clinical characteristics of left ventricular dysfunction among elderly patients in general practice setting: Cross sectional survey. *BMJ*. 1999;318(7180):368-372.
14. Gillespie ND, McNeill G, Pringle T, Ogston S, Struthers AD, Pringle SD. Cross sectional study of contribution of clinical assessment and simple cardiac investigations to diagnosis of left ventricular systolic dysfunction in patients admitted with acute dyspnoea. *BMJ*. 1997;314(7085):936-940.
15. Badgett RG, Mulrow CD, Otto PM, Ramirez G. How well can the chest radiograph diagnose left ventricular dysfunction? *J Gen Intern Med*. 1996;11(10):625-634.
16. Knudsen CW, Omland T, Clopton P, et al. Diagnostic value of B-Type natriuretic peptide and chest radiographic findings in patients with acute dyspnea. *Am J Med*. 2004;116(6):363-368.
17. Davie AP, Francis CM, Love MP, et al. Value of the electrocardiogram in identifying heart failure due to left ventricular systolic dysfunction. *BMJ*. 1996;312(7025):222.
18. Erbel R, Schweizer P, Krebs W, Meyer J, Effert S. Sensitivity and specificity of two-dimensional

echocardiography in detection of impaired left ventricular function. *Eur Heart J*. 1984;5(6):477-489.
19. Vigna C, Russo A, De Rito V, et al. Regional wall motion analysis by dobutamine stess echocardiography to distinguish between ischemic and nonischemic dilated cardiomyopathy. *Am Heart J*. 1996;131(3):537-543.
20. Naqvi TZ, Goel RK, Forrester JS, Siegel RJ. Myocardial contractile reserve on dobutamine echocardiography predicts late spontaneous improvement in cardiac function in patients with recent onset idiopathic dilated cardiomyopathy. *J Am Coll Cardiol*. 1999;34(5):1537-1544.
21. Naqvi TZ, Goel RK, Forrester JS, Davidson RM, Siegel RJ. Usefulness of left ventricular mass in predicting recovery of left ventricular systolic function in patients with symptomatic idiopathic dilated cardiomyopathy. *Am J Cardiol*. 2000;85(5):624-629.
22. Felker GM, Thompson RE, Hare JM, et al. Underlying causes and long-term survival in patients with initially unexplained cardiomyopathy. *N Engl J Med*. 2000;342(15):1077-1084.
23. Scanlon PJ, Faxon DP, Audet AM, et al. ACC/AHA guidelines for coronary angiography: Executive summary and recommendations. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Coronary Angiography) developed in collaboration with the Society for Cardiac Angiography and Interventions. *Circulation*. 1999;99(17):2345-2357.
24. Starling RC, Van Fossen DB, Hammer DF, Unverferth DV. Morbidity of endomyocardial biopsy in cardiomyopathy. *Am J Cardiol*. 1991;68(1):133-136.
25. Mason JW. Endomyocardial biopsy and the causes of dilated cardiomyopathy. *J Am Coll Cardiol*. 1994;23(3):591-592.
26. Cohn JN. Structural basis for heart failure. Ventricular remodeling and its pharmacological inhibition. *Circulation*. 1995;91(10):2504-2507.
27. Lee KS, Marwick TH, Cook SA, et al. Prognosis of patients with left ventricular dysfunction, with and without viable myocardium after myocardial infarction. Relative efficacy of medical therapy and revascularization. *Circulation*. 1994;90(6):2687-2694.
28. Gioia G, Powers J, Heo J, Iskandrian AS. Prognostic value of rest-redistribution tomographic thallium-201 imaging in ischemic cardiomyopathy. *Am J Cardiol*. 1995;75(12):759-762.
29. Pagley PR, Beller GA, Watson DD, Gimple LW, Ragosta M. Improved outcome after coronary bypass surgery in patients with ischemic cardiomyopathy and residual myocardial viability. *Circulation*. 1997;96(3):793-800.
30. Baer FM, Theissen P, Schneider CA, et al. Dobutamine magnetic resonance imaging predicts contractile recovery of chronically dysfunctional myocardium after successful revascularization. *J Am Coll Cardiol*. 1998;31(5):1040-1048.
31. Wellnhofer E, Olariu A, Klein C, et al. Magnetic resonance low-dose dobutamine test is superior to SCAR quantification for the prediction of functional recovery. *Circulation*. 2004;109(18):2172-2174.
32. Bax JJ, Poldermans D, Elhendy A, et al. Improvement of left ventricular ejection fraction, heart failure symptoms and prognosis after revascularization in patients with chronic coronary artery disease and viable myocardium detected by dobutamine stress echocardiography. *J Am Coll Cardiol*. 1999;34(1):163-169.
33. Pfeffer MA, Braunwald E, Moye LA, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. *N Engl J Med*. 1992;327(10):669-677.
34. Effect of ramipril on mortality and morbidity of survivors of acute myocardial infarction with clinical evidence of heart failure. The Acute Infarction Ramipril Efficacy (AIRE) Study Investigators. *Lancet*. 1993;342(8875):821-828.
35. Kober L, Torp-Pedersen C, Carlsen JE, et al. A clinical trial of the angiotensin-converting-enzyme inhibitor trandolapril in patients with left ventricular dysfunction after myocardial infarction. Trandolapril Cardiac Evaluation (TRACE) Study Group. *N Engl J Med*. 1995;333(25):1670-1676.
36. CIBIS Investigators and Committees A randomized trial of beta-blockade in heart failure. The Cardiac Insufficiency Bisoprolol Study (CIBIS). *Circulation*. 1994;90(4):1765-1773.
37. The Cardiac Insufficiency Bisoprolol Study II (CIBIS-II): A randomised trial. *Lancet*. 1999;353(9146):9-13.
38. Effect of metoprolol CR/XL in chronic heart failure: Metoprolol CR/XL Randomised Intervention Trial in Congestive Heart Failure (MERIT-HF). *Lancet*. 1999;353(9169):2001-2007.
39. Packer M, Bristow MR, Cohn JN, et al. The effect of carvedilol on morbidity and mortality in patients with chronic heart failure. U.S. Carvedilol Heart Failure Study Group. *N Engl J Med*. 1996;334(21):1349-1355.
40. Yancy CW, Fowler MB, Colucci WS, et al. Race and the response to adrenergic blockade with carvedilol in patients with chronic heart failure. *N Engl J Med*. 2001;344(18):1358-1365.
41. Aikawa Y, Rohde L, Plehn J, et al. Regional wall stress predicts ventricular remodeling after anteroseptal myocardial infarction in the Healing and Early Afterload Reducing Trial (HEART): An

echocardiography-based structural analysis. *Am Heart J*. 2001;141(2):234-242.
42. Konstam MA, Kronenberg MW, Rousseau MF, et al. Effects of the angiotensin converting enzyme inhibitor enalapril on the long-term progression of left ventricular dilatation in patients with asymptomatic systolic dysfunction. SOLVD (Studies of Left Ventricular Dysfunction) Investigators. *Circulation*. 1993;88(suppl 5, pt 1):2277-2283.
43. Australia/New Zealand Heart Failure Research Collaborative Group. Randomised, placebo-controlled trial of carvedilol in patients with congestive heart failure due to ischaemic heart disease. *Lancet*. 1997;349(9049):375-380.
44. Abraham WT, Fisher WG, Smith AL, et al. Cardiac resynchronization in chronic heart failure. *N Engl J Med*. 2002;346(24):1845-1853.
45. Cazeau S, Leclercq C, Lavergne T, et al. Effects of multisite biventricular pacing in patients with heart failure and intraventricular conduction delay. *N Engl J Med*. 2001;344(12):873-880.
46. Batista RJ, Santos JL, Takeshita N, Bocchino L, Lima PN, Cunha MA. Partial left ventriculectomy to improve left ventricular function in end-stage heart disease. *J Card Surg*. 1996;11(2):96-97; discussion 8.
47. Batista RJ, Verde J, Nery P, et al. Partial left ventriculectomy to treat end-stage heart disease. *Ann Thorac Surg*. 1997;64(3):634-638.
48. Schreuder JJ, Steendijk P, van der Veen FH, et al. Acute and short-term effects of partial left ventriculectomy in dilated cardiomyopathy: Assessment by pressure-volume loops. *J Am Coll Cardiol*. 2000;36(7):2104-2114.
49. Etoch SW, Koenig SC, Laureano MA, Cerrito P, Gray LA, Dowling RD. Results after partial left ventriculectomy versus heart transplantation for idiopathic cardiomyopathy. *J Thorac Cardiovasc Surg*. 1999;117(5):952-959.
50. Angelini GD, Pryn S, Mehta D, et al. Left-ventricular-volume reduction for end-stage heart failure. *Lancet*. 1997;350(9076):489.
51. Franco-Cereceda A, McCarthy PM, Blackstone EH, et al. Partial left ventriculectomy for dilated cardiomyopathy: Is this an alternative to transplantation? *J Thorac Cardiovasc Surg*. 2001;121(5):879-893.
52. Moreira LF, Stolf NA, Bocchi EA, et al. Partial left ventriculectomy with mitral valve preservation in the treatment of patients with dilated cardiomyopathy. *J Thorac Cardiovasc Surg*. 1998;115(4):800-807.
53. Bestetti RB, Moreira-Neto F, Brasil JC, Bombonato R, Sgarbieri RN, Haddad J. Partial left ventriculectomy: Preoperative risk factors for perioperative mortality. *Int J Cardiol*. 1998;67(2):143-146.
54. Gradinac S, Miric M, Popovic Z, et al. Partial left ventriculectomy for idiopathic dilated cardiomyopathy: Early results and six-month follow-up. *Ann Thorac Surg*. 1998;66(6):1963-1968.
55. Stolf NA, Moreira LF, Bocchi EA, et al. Determinants of midterm outcome of partial left ventriculectomy in dilated cardiomyopathy. *Ann Thorac Surg*. 1998;66(5):1585-1591.
56. McCarthy JF, McCarthy PM, Starling RC, et al. Partial left ventriculectomy and mitral valve repair for end-stage congestive heart failure. *Eur J Cardiothorac Surg*. 1998;13(4):337-343.
57. Starling RC, McCarthy PM, Buda T, et al. Results of partial left ventriculectomy for dilated cardiomyopathy: Hemodynamic, clinical and echocardiographic observations. *J Am Coll Cardiol*. 2000;36(7):2098-2103.
58. Dor V. Left ventricular aneurysms: The endoventricular circular patch plasty. *Semin Thorac Cardiovasc Surg*. 1997;9(2):123-130.
59. Froehlich RT, Falsetti HL, Doty DB, Marcus ML. Prospective study of surgery for left ventricular aneurysm. *Am J Cardiol*. 1980;45(5):923-931.
60. Di Donato M, Sabatier M, Dor V, et al. Effects of the Dor procedure on left ventricular dimension and shape and geometric correlates of mitral regurgitation one year after surgery. *J Thorac Cardiovasc Surg*. 2001;121(1):91-96.
61. Di Donato M, Sabatier M, Dor V, Toso A, Maioli M, Fantini F. Akinetic versus dyskinetic postinfarction scar: Relation to surgical outcome in patients undergoing endoventricular circular patch plasty repair. *J Am Coll Cardiol*. 1997;29(7):1569-1575.
62. Dor V, Saab M, Coste P, Sabatier M, Montiglio F. Endoventricular patch plasties with septal exclusion for repair of ischemic left ventricle: Technique, results and indications from a series of 781 cases. *Jpn J Thorac Cardiovasc Surg*. 1998;46(5):389-398.
63. Menicanti L, Di Donato M. The Dor procedure: What has changed after fifteen years of clinical practice? *J Thorac Cardiovasc Surg*. 2002;124(5):886-890.
64. Kaza AK, Patel MR, Fiser SM, et al. Ventricular reconstruction results in improved left ventricular function and amelioration of mitral insufficiency. *Ann Surg*. 2002;235(6):828-832.
65. Maxey TS, Reece TB, Ellman PI, Kern JA, Tribble CG, Kron IL. The beating heart approach is not necessary for the Dor procedure. *Ann Thorac Surg*. 2003;76(5):1571–1574; discussion 4-5.
66. Cope JT, Kaza AK, Reade CC, et al. A cost comparison of heart transplantation versus alternative operations for cardiomyopathy. *Ann Thorac Surg*. 2001;72(4):1298-1305.

DropBooks

67. Izumi S, Miyatake K, Beppu S, et al. Mechanism of mitral regurgitation in patients with myocardial infarction: A study using real-time two-dimensional Doppler flow imaging and echocardiography. *Circulation*. 1987;76(4):777-785.
68. Kono T, Sabbah HN, Rosman H, Alam M, Jafri S, Goldstein S. Left ventricular shape is the primary determinant of functional mitral regurgitation in heart failure. *J Am Coll Cardiol*. 1992;20(7):1594-1598.
69. Yoran C, Yellin EL, Becker RM, Gabbay S, Frater RW, Sonnenblick EH. Dynamic aspects of acute mitral regurgitation: Effects of ventricular volume, pressure and contractility on the effective regurgitant orifice area. *Circulation*. 1979;60(1):170-176.
70. Blondheim DS, Jacobs LE, Kotler MN, Costacurta GA, Parry WR. Dilated cardiomyopathy with mitral regurgitation: Decreased survival despite a low frequency of left ventricular thrombus. *Am Heart J*. 1991;122(suppl 3, pt 1):763-771.
71. Chen FY, Adams DH, Aranki SF, et al. Mitral valve repair in cardiomyopathy. *Circulation*. 1998;98(suppl 19):II124-II1277.
72. Cohn LH, Rizzo RJ, Adams DH, et al. The effect of pathophysiology on the surgical treatment of ischemic mitral regurgitation: Operative and late risks of repair versus replacement. *Eur J Cardiothorac Surg*. 1995;9(10):568-574.
73. Bolling SF, Deeb GM, Brunsting LA, Bach DS. Early outcome of mitral valve reconstruction in patients with end-stage cardiomyopathy. *J Thorac Cardiovasc Surg*. 1995;109(4):676–682; discussion 82-83.
74. Bolling SF, Pagani FD, Deeb GM, Bach DS. Intermediate-term outcome of mitral reconstruction in cardiomyopathy. *J Thorac Cardiovasc Surg*. 1998;115(2):381–386; discussion 7-8.
75. Smolens IA, Pagani FD, Bolling SF. Mitral valve repair in heart failure. *Eur J Heart Fail*. 2000;2(4):365-371.
76. Sintek CF, Pfeffer TA, Kochamba G, Fletcher A, Khonsari S. Preservation of normal left ventricular geometry during mitral valve replacement. *J Heart Valve Dis*. 1995;4(5):471–475; discussion 5-6.
77. Sarris GE, Cahill PD, Hansen DE, Derby GC, Miller DC. Restoration of left ventricular systolic performance after reattachment of the mitral chordae tendineae. The importance of valvular-ventricular interaction. *J Thorac Cardiovasc Surg*. 1988;95(6):969-979.
78. Natsuaki M, Itoh T, Tomita S, et al. Importance of preserving the mitral subvalvular apparatus in mitral valve replacement. *Ann Thorac Surg*. 1996;61(2):585-590.
79. Komeda M, David TE, Rao V, Sun Z, Weisel RD, Burns RJ. Late hemodynamic effects of the preserved papillary muscles during mitral valve replacement. *Circulation*. 1994;90(5 Pt 2):II190-II194.
80. Cohn LH, Couper GS, Kinchla NM, Collins JJ, Jr. Decreased operative risk of surgical treatment of mitral regurgitation with or without coronary artery disease. *J Am Coll Cardiol*. 1990;16(7):1575-1578.
81. Gangemi JJ, Tribble CG, Ross SD, McPherson JA, Kern JA, Kron IL. Does the additive risk of mitral valve repair in patients with ischemic cardiomyopathy prohibit surgical intervention? *Ann Surg*. 2000;231(5):710-714.
82. Sheiban I, Tonni S, Marini A, Trevi G. Clinical and therapeutic implications of chronic left ventricular dysfunction in coronary artery disease. *Am J Cardiol*. 1995;75(13):23E-30E.
83. Ragosta M, Beller GA, Watson DD, Kaul S, Gimple LW. Quantitative planar rest-redistribution 201Tl imaging in detection of myocardial viability and prediction of improvement in left ventricular function after coronary bypass surgery in patients with severely depressed left ventricular function. *Circulation*. 1993;87(5):1630-1641.
84. Pagano D, Bonser RS, Camici PG. Myocardial revascularization for the treatment of post-ischemic heart failure. *Curr Opin Cardiol*. 1999;14(6):506-509.
85. Trachiotis GD, Weintraub WS, Johnston TS, Jones EL, Guyton RA, Craver JM. Coronary artery bypass grafting in patients with advanced left ventricular dysfunction. *Ann Thorac Surg*. 1998;66(5):1632-1639.
86. Dreyfus GD, Duboc D, Blasco A, et al. Myocardial viability assessment in ischemic cardiomyopathy: Benefits of coronary revascularization. *Ann Thorac Surg*. 1994;57(6):1402–1407; discussion 7-8.
87. Tjan TD, Kondruweit M, Scheld HH, et al. The bad ventricle—Revascularization versus transplantation. *Thorac Cardiovasc Surg*. 2000;48(1):9-14.
88. Lansman SL, Cohen M, Galla JD, et al. Coronary bypass with ejection fraction of 0.20 or less using centigrade cardioplegia: Long-term follow-up. *Ann Thorac Surg*. 1993;56(3):480–485; discussion 5-6.
89. Kaul TK, Agnihotri AK, Fields BL, Riggins LS, Wyatt DA, Jones CR. Coronary artery bypass grafting in patients with an ejection fraction of twenty percent or less. *J Thorac Cardiovasc Surg*. 1996;111(5):1001-1012.
90. Bolling SF, Smolens IA, Pagani FD. Surgical alternatives for heart failure. *J Heart Lung Transplant* 2001;20(7):729-733.
91. Aziz T, Burgess M, Rahman AN, Campbell CS, Yonan N. Cardiac transplantation for cardiomyopathy and ischemic heart disease: Differences in outcome up to 10 years. *J Heart Lung Transplant*. 2001;20(5):525-533.
92. Maxey TS, Reece TB, Ellman PI, et al. Coronary artery bypass with ventricular restoration is superior

to coronary artery bypass alone in patients with ischemic cardiomyopathy. *J Thorac Cardiovasc Surg*. 2004;127(2):428-434.
93. Runyan S, Dobie S. CABG compared with PTCA in heart disease. *J Fam Pract*. 1998;46(2):112-113.
94. Gibbons RJ, Chatterjee K, Daley J, et al. ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Chronic Stable Angina). *J Am Coll Cardiol*. 1999;33(7):2092-2197.
95. Ogletree-Hughes ML, Stull LB, Sweet WE, Smedira NG, McCarthy PM, Moravec CS. Mechanical unloading restores beta-adrenergic responsiveness and reverses receptor downregulation in the failing human heart. *Circulation*. 2001;104(8):881-886.
96. Heerdt PM, Holmes JW, Cai B, et al. Chronic unloading by left ventricular assist device reverses contractile dysfunction and alters gene expression in end-stage heart failure. *Circulation*. 2000;102(22):2713-2719.
97. Bruckner BA, Stetson SJ, Perez-Verdia A, et al. Regression of fibrosis and hypertrophy in failing myocardium following mechanical circulatory support. *J Heart Lung Transplant*. 2001;20(4):457-464.
98. Vatta M, Stetson SJ, Perez-Verdia A, et al. Molecular remodelling of dystrophin in patients with end-stage cardiomyopathies and reversal in patients on assistance-device therapy. *Lancet* 2002;359(9310):936-941.
99. Pennington DG, Swartz MT. Mechanical circulatory support prior to cardiac transplantation. *Semin Thorac Cardiovasc Surg*. 1990;2(2):125-134.
100. Rose EA, Gelijns AC, Moskowitz AJ, et al. Long-term mechanical left ventricular assistance for end-stage heart failure. *N Engl J Med*. 2001;345(20):1435-1443.
101. Dor V, Sabatier M, Di Donato M, Montiglio F, Toso A, Maioli M. Efficacy of endoventricular patch plasty in large postinfarction akinetic scar and severe left ventricular dysfunction: Comparison with a series of large dyskinetic scars. *J Thorac Cardiovasc Surg*. 1998;116(1):50-59.
102. Acker MA. Dynamic cardiomyoplasty: At the crossroads. *Ann Thorac Surg*. 1999;68(2):750–755.
103. Hayward MP. Dynamic cardiomyoplasty: Time to wrap it up? *Heart*. 1999;82(3):263-264.
104. 50th Annual Scientific Session of the American College of Cardiology. Orlando, Florida, USA. March 18–21, 2001. *J Am Coll Cardiol*. 2001;37(2 Suppl A):1A-647A.
105. Hosenpud JD, Bennett LE, Keck BM, Fiol B, Boucek MM, Novick RJ. The Registry of the International Society for Heart and Lung Transplantation: Sixteenth official report—1999. *J Heart Lung Transplant*. 1999;18(7):611-626.
106. Steinman TI, Becker BN, Frost AE, et al. Guidelines for the referral and management of patients eligible for solid organ transplantation. *Transplantation*. 2001;71(9):1189-1204.

DropBooks

4
Advanced Heart Failure:
Transplant vs Nontransplant Surgical Options

Stephen Westaby and Gabriele Bertoni

4.1. Introduction

Advanced heart failure is a desperately debilitating and frightening condition. Successful intervention in acute coronary syndromes together with improved management of idiopathic dilated cardiomyopathy and dysrrhythmia provide an ever-increasing number of advanced heart failure patients spread over a wide age range. Young adults with surgically palliated congenital heart disease enter the lower end of the spectrum. Many patients have relentlessly worsening symptoms and very poor quality of life.

Ten percent of heart failure patients are categorized Stage D [New York Heart Association (NYHA) class IV] with advanced structural heart disease and marked symptoms at rest despite detailed medical or resynchronization therapy. These patients become progressively more dependent on hospital admissions for symptomatic stabilization and outpatient nursing for palliative care. Currently, there are more than 300,000 Stage D patients in the USA and 60,000 in the UK. Twenty percent are under 65 years of age (60,000 USA, 12,000 UK, respectively). This constitutes a massive financial burden without providing significant prognostic improvement. Nevertheless, most civilized societies are prepared to invest in both drugs and devices to relieve symptoms and improve the quality and duration of life within reasonable limits. These limits are largely set by age considerations and economics rather than the ethical dilemmas surrounding a particular intervention. A precedent has been set by the management of end-stage renal disease. Hemodialysis is currently offered without age limits to the majority of patients, providing around 60% 2-year survival. Renal transplantation is offered to selected patients younger than 75 years of age without significant comorbidity. In contrast there are no temporizing measures for hepatic failure. Either the patient is accepted for transplantation and receives a donor liver or death ensues. Until recently the treatment of heart failure was comparable with that of liver disease. In many countries (including the UK) mechanical circulatory support technology is still not made available by the health care system.

Cardiac transplantation provides a very exciting and effective treatment with survival exceeding 80% at 1 year and almost 50% at 10 years.[1] However, by the very nature of heart failure, 80% of patients are over 65 years of age and the vast majority of younger patients have important comorbidity. Within the rigorous selection criteria, these factors effectively preclude transplantation. Given a progressive fall in donor availability (currently around 2,200 and 150 hearts, respectively, per year in the USA and UK), these limitations have allowed uncontroversial cost containment in the treatment of advanced heart disease[2] to the extent that Adamson in his paper "The Evolving Challenge of Heart Failure Management" describes heart transplantation as an epidemiologically insignificant intervention.[3] Accordingly, the development of nontransplant surgical options and their widespread adoption is a clear priority.

The goal of both medical and surgical treatment is to arrest or reverse the progression of the cardiac

remodeling process. Currently there are a few guidelines as to which treatment best suits an individual patient or pathological process. An evidence-based approach can only be achieved using detailed investigation and clinical measurement to identify the pathological process and determine the extent of structural and functional abnormalities. The object of investigation is to establish whether there is a lesion amenable for surgical repair, whether dysfunctional myocardium is potentially recoverable, or, in the event of neither of these, whether the complete cardiac replacement or mechanical left ventricular assist are feasible. Left ventricular shape and volume are important predictors of survival. In both ischemic and idiopathic dilated cardiomyopathy, increased chambers sphericity and the onset of mitral regurgitation are markers of worse prognosis (1-year mortality 54–70%).[4] Mitral regurgitation occurs secondary to altered left ventricular geometry, papillary muscle dysfunction, and annular dilatation. Volume overload causes progressive left ventricular dilatation, worsened mitral regurgitation, and decreased survival. Patients with the left ventricular ejection fraction (LVEF) of less than 30% have a 5-year survival of only 54% when the left ventricular end-systolic volume index (LVESVI) exceeds 150 ml/m^2.[5]

Although the prognostic implications of progressive left ventricular remodeling are clearly understood, there are no clear guidelines or algorithm to indicate which cardiological or surgical intervention best suits a particular patient. Guidelines from the National Institute for Clinical Excellence (UK 2004) for "Best Practice in Chronic Heart Failure" make only brief reference to surgery in the vaguest terms: "Coronary revascularization should not be routinely considered in heart failure due to systolic left ventricular impairment unless the patient has refractory angina" and "Specialist referral for transplantation should be considered in patients with refractory symptoms or cardiogenic shock."[6] After the very important developments in the nontransplant surgery of heart failure over the last 10 years, there is a clear requirement to establish the surgeon's role in relieving symptoms and improving prognosis for an individual patient with defined pathology. Given the limits of transplantation, it may well be preferable to repair rather than replace the diseased heart but the role of individual procedures (interventional cardiology and surgery) must be clearly defined. This chapter is about choices. Whether to treat, how to treat, and when to treat.

4.2. How Does the Heart Failure Patient Reach the Surgeon

There are often three tiers of medical care before surgical assessment. A patient with the symptoms and clinical signs of heart failure first presents to the primary care physician who may instigate medical therapy. It can be difficult to determine the cause of left ventricular dysfunction. In one study in Glasgow (UK), 95% of symptomatic and 71% of asymptomatic patients with left ventricular systolic dysfunction had evidence of coronary artery disease.[7] Those with symptomatic heart failure were more likely to have a previous myocardial infarction (50% vs 14%) and concurrent angina (62% vs 43%) Hypertension was also present in 80% of those with symptomatic heart failure. In the Italian Studio sull' Epidemiologia Ospedaliera dello Scompenso in Italia or Survey on Heart Failure in Italian Hospital Cardiology Units (SEOSI) study, 70% of patients had a previous myocardial infarction whereas 15% had hypertensive heart disease.[8] Idiopathic dilated cardiomyopathy and valvular heart disease each accounted for 15% of patients.

Age has a varying influence in different health care systems. In the elderly further referral may not be considered unless a murmur (valvular heart disease) is detected or the patient has angina. Patients younger than 75 years are generally referred to a local cardiologist to define the etiology and the extent of left ventricular dysfunction. Echocardiography and coronary angiography are usually performed at this stage to differentiate between ischemic, restrictive, or idiopathic dilated cardiomyopathy.

The local cardiologist directs further management by tertiary referral to an interventional cardiologist or surgeon with heart failure expertise, an electrophysiologist when dysrrhythmia is the problem, or a transplant center if the patient is severely symptomatic and (conventionally) less than 65 years of age. As a result the patient may proceed to revascularization, receive either an implantable defibrillator or cardiac resynchronization therapy, or be assessed regarding eligibility for transplantation. In the authors' experience, few patients are referred for conventional surgical assessment in a timely fashion, and the awareness of the nontransplant surgical options is limited. Ischemic heart disease is responsible

DropBooks

for two-thirds of end-stage heart failure patients, and hibernating myocardium, anterolateral or septal scar, and mitral regurgitation are each amenable to surgical repair. Similarly patients with idiopathic dilated cardiomyopathy, a remodeled ventricle, and worsening mitral regurgitation may benefit from mitral valve repair or external constraint. Even in the absence of a target lesion, a nontransplant eligible patient can be considered for long-term mechanical circulatory support as definitive treatment or possibly to reverse the remodeling process sufficient to allow removal of the device.[9]

In advanced heart failure, specialized treatment centers that provide frequent follow-up and organized delivery of care can dramatically reduce the rate of readmission and length of stay during periods of decompensation. Given the greater diversity of operative procedures, the surgery of advanced heart failure must evolve into a discrete specialty. There is justification for all Stage C and D patients to be jointly assessed by a multidisciplinary heart failure team, including the surgeon. Allocation to the appropriate intervention needs very detailed definition of coronary anatomy, myocardial structure, dynamic dimensions, ventricular function, viability, and the potential for improvement. Significant comorbidity, particularly renal and hepatic status, must be taken into consideration before deciding upon a particular procedure. The surgeon's role is to determine which operation or combination of surgical procedures best suits an individual and whether surgeons can undertake an acceptable risk with likelihood of benefit given the clinical status of the patient. Many are left too late for revascularization of hibernating myocardium or left ventricular restoration surgery to improve symptoms or prognosis. The surgeon should recognize the limits of each procedure and operate only when optimization of medical treatment has provided the best setting for recovery. In general, nontransplant options should always be considered first and carried out in such a way that a cardiac transplant or mechanical circulatory support remain feasible in the future.

4.3. How to Determine the Surgical Strategy

The treatment adopted depends upon the etiology of heart failure, the clinical stage, the cardiac dimensions, the presence of a target lesion amenable to surgery, and the potential to improve left ventricular function (Figure 4.1). Eligibility for

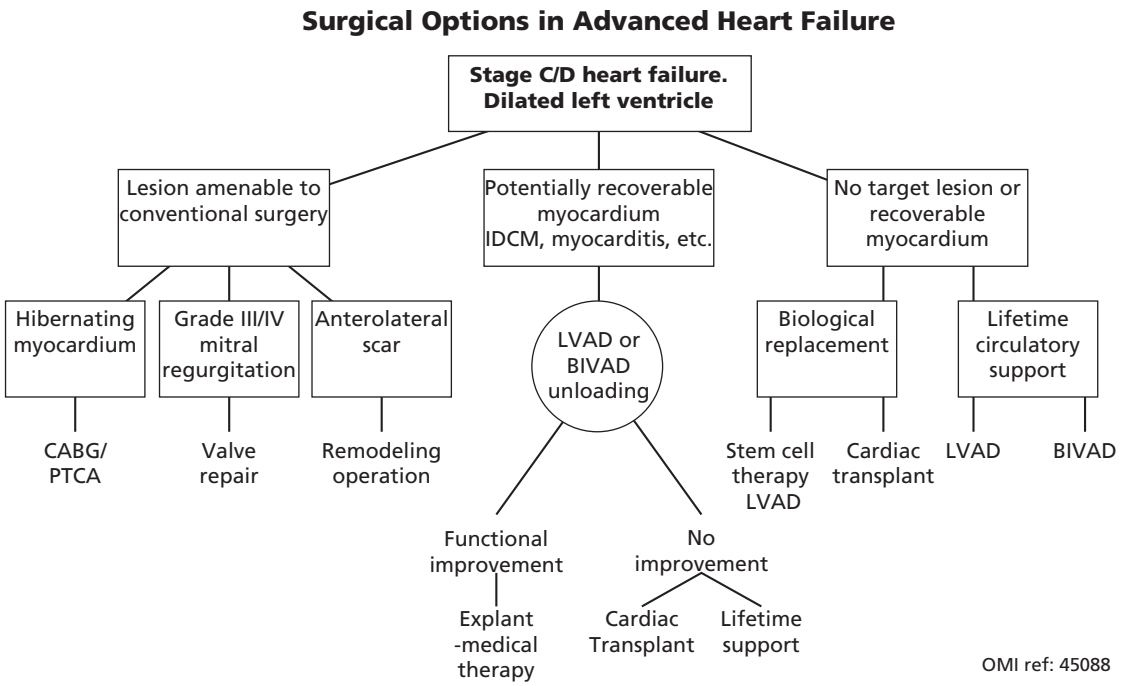


FIGURE 4.1. Algorithm outlining the decision-making process in an advanced heart failure patient. Repair is considered before replacement.

cardiac transplantation is determined during the course of medical assessment, and committal to a transplant waiting list should occur only when other avenues have been exhausted.

At the time of surgical assessment most patients are Stage C or D with a dilated left ventricle and impaired cardiac output. For patients who present in cardiogenic shock with either acute or decompensated chronic cardiac failure, urgent mechanical circulatory support may be necessary pending diagnosis, further assessment, and definitive treatment. Detailed cardiac assessment is supported by careful determination of other risk factors including age and respiratory, vascular, renal, and hepatic dysfunction. A bank of a clinical investigations including coronary angiography, echocardiography, magnetic resonance imaging (MRI), assessment of myocardial viability and functional assessment by six-minute walk test, and measurement of mixed venous oxygen content on exercise (MVO_2) provide the required information about cardiac pathophysiology and functional status.[10] On the basis of these findings, the multidisciplinary team should decide whether there is a lesion amenable to conventional surgery, or potentially recoverable myocardium (stunning, hibernation, idiopathic dilated cardiomyopathy, or myocarditis) or indeed, whether there is no possibility of a nontransplant surgical route. This leaves cardiac replacement or long-term circulatory support as the only option.

The medical and surgical options, their risks, and potential benefits can then be discussed with the patient.

4.4. Decision-Making in Patients with Ischemic Cardiomyopathy

4.4.1. The Mechanisms of Ischemic Cardiomyopathy

At the onset of heart failure, the goal of both medical and surgical treatment is to prevent progression of the remodeling process. Surgical strategies take into account the LaPlace law which estimates myocardial wall stress from left ventricular pressure, radius of cavity, and wall thickness. The enlarged chamber radius of the failing heart exposes myocytes to increased systolic wall stress. Molecular proliferative responses then lead to cellular and chamber hypertrophy. The ischemic cardiomyopathy ventricle contains microenvironments of irreversibly injured myocytes with necrosis or scar tissue, together with viable myocardial cells in varying proportions. This pattern is evident from intraoperative inspection and from the change from akinesia to hypokinesia or normal wall motion in some left ventricular wall segments after percutaneous transluminal coronary angioplasty (PTCA) or coronary artery bypass grafting (CABG). These ischemic morphological changes within the myocardium are self-aggravating because of their effects on blood flow to the subendocardial layer. Repeated infarction cause more scarring. Eventually, left ventricular systolic and diastolic dysfunction produce the syndrome of congestive heart failure. Alternatively, patients with left ventricular dysfunction die suddenly from further infarction or ventricular fibrillation triggered by ischemic myocardium.

The degree of left ventricular dysfunction has a well-defined impact on survival. When the dyskinetic region occupies more than 20% of the total myocardial mass (40% of all transmural myocardial infarction), the left ventricle progressively enlarges with the onset of symptomatic heart failure. When more then 50% of the myocardium is impaired, increased wall tension causes subendocardial ischemia in the remote myocardium. This triggers left ventricular failure. The relationship between the extent of myocardial infarction, degree of left ventricular dysfunction, and late mortality was defined by Yoshida and Gould.[11] They showed that a myocardial infarction greater than 23% of the left ventricular circumference caused impaired LVEF (<45%) and the 3-year mortality rate exceeded 40% (Table 4.1). This contrasted with less extensive myocardial infarction, which resulted in a 3-year mortality rate of only 5%. For patients in whom the LVEF was <43%, the 3-year mortality rate was 38% in contrast to only 6% when LVEF was >43%. However, LVEF alone is a poor predictor of mortality in patients with hibernating myocardium. The presence of viable myocardium is an independent predictor of survival as well as a marker for those with impaired LVEF who are most likely to benefit from revascularization. The 3-year mortality rate in patients with an LVEF of <43% and no viable myocardium was 63%, in contrast to 13% for those with viable myocardium submitted

DropBooks

TABLE 4.1. Impact of the extent of ischemic myocardial injury on patient survival.

	Three-year mortality (%)	*p* Value
Myocardial infarction or scar of ≥23%	43	0.014
Myocardial infarction or scar of <23%	5	
EF < 43%	38	0.029
EF > 43%	6	
EF ≤ 43% without viable myocardium	63	0.059
EF ≤ 43% with viable myocardium[a]	13	

[a]For all patients with viable myocardium, the 3-year mortality rate was 8% (80% had CABG). For patients with only fixed scar of >23%, mortality rate was 50% (p = 0.018, only 40% had CABG).[11]

EF ejection fraction.

© 2007 by American College of Cardiology Foundation.

for revascularization. For patients with only scar in the territory at risk from coronary occlusion, the mortality rate of 50% at 3 years was not different with or without revascularization, indicating no benefit from intervention in this subgroup.

The components of postinfarction left ventricular remodeling include infarct expansion, myocardial hypertrophy, and global left ventricular dilatation resulting in a more spherical contour. The workload of myocardium remote from the akinetic or dyskinetic area is increased by the dysfunctional changes. Increased wall stress results in lengthening and thinning of the LV walls through lateral slippage of myocardial planes. The changes in ventricular geometry, local wall tension, and filling pressures combined to increase the metabolic requirements of nonischemic myocardium, which plays a critical part in maintaining cardiac output. Working segments undergo compensatory hypertrophy. A low LVEF (<30%) indicates that the ventricle has remodeled but a dilated chamber with low LVEF can eject the same stroke volume as a ventricle with an LVEF of 60%. A decrease in LVEF does not necessarily reflect an impairment of contraction but rather a remodeling of the ventricle. Exercise capacity has a poor relationship with LV function although LVEF is an important determinant for survival. Patients with an LVEF of >40% have modest annual mortality rate (<10%) whereas those with an LVEF of <30% have annual mortality rates of >25%.[12] In patients with an LVEF of 15–40%, there is an association between LVEF and annual mortality rate.

Abnormalities of left ventricular diastolic function can be demonstrated during stress in most patients with extensive coronary disease. These are manifest by a reduced peak left ventricular filling rate and increased time-to-peak filling rate. Hypoxia impairs relaxation of the papillary muscles because myocardial relaxation during early diastole is an active energy-dependent process. Ischemic abnormalities of left ventricular systolic and diastolic function may be sufficiently severe during stress to cause substantially elevated LV end-diastolic pressure (LVEDP). This results in dyspnea as well as angina during the ischemic episode. Impairment of left ventricular function at rest may be the results of myocardial scar, stunning, or hibernation. Commonly, dysfunction occurs through a combination of these entities within the same heart. Some patients have moderately increased LVEDP at rest with considerably reduced exercise capacity, but only a mildly increased cardiac size on chest radiography. These patients often have moderate scaring and marked ischemic dysfunction in nonscarred parts of the ventricles, and may be helped by revascularization. Others have moderate or severe cardiomegaly, reduced cardiac index, and substantial elevation of right atrial pressure with hepatomegaly and fluid retention. This latter group usually has extensive myocardial scarring and is unlikely to improve by revascularization alone.

The relationship between myocardial stunning, hibernation, and heart failure remains complex. Some patients with coronary disease do not stun, whereas others suffer repeated clinically silent episode of stunning during normal daily activities. If such episodes are frequent with incomplete recovery of contractile function before the next insult, then chronic ventricular dysfunction may ensue. Repetitive stunning may trigger the development of myocardial hibernation, which is associated with changes in myocyte metabolism and structure.[13] Structural changes depend on the time that myocardial blood supply remains jeopardized during demand ischemia. Thus, myocardium may progress through a phase of functional hibernation (without changes in the contractile protein apparatus) to a phase of structural hibernation with morphological abnormalities within the myocyte, including loss of myofibrillar material and accumulation of glycogen.[14]

In structural hibernation, functional recovery after revascularization is more prolonged and dependent on new protein synthesis and myocyte repair. In the absence of revascularization, repetitive ischemia may progress to myocyte necrosis or apoptosis, indicating that hibernating myocardium is not fully adapted to chronic hypoperfusion. Cellular degeneration and myocyte loss are accompanied by reparative fibrosis. They combine to cause degeneration in the structural and functional integrity of the left ventricle, even in the absence of myocardial infarction. Consequently, if revascularization is to succeed, it must be applied early before functional hibernation progresses to structural hibernation. Hibernating myocardium is present in about 78% of patients after myocardial infarction treated by thrombolysis.[15] Cardiac events including death, nonfatal myocardial infarction, or unstable angina occur in 33% of patients with hibernation, versus only 8% for those with scar.[16]

4.4.2. Coronary Bypass or Transplantation?

The different pathways toward myocardial revascularization or cardiac transplantation need careful consideration. The vast majority of patients with ischemic cardiomyopathy are older than 65 years, are smokers with chronic obstructive airways disease, and have peripheral vasculopathy. They often have renal impairment and will never be considered for transplantation. Less than 10% of potential heart transplant candidates (referred as opposed to selected for the waiting list) will eventually receive a donor organ.

Recent studies suggest that as many as 50% of coronary patients referred for transplantation have hibernating myocardium.[17] In an attempt to lower waiting list mortality and provide an alternative to transplantation, many centers now select non–inotrope-dependent patients for “higher risk” coronary artery bypass with or without left ventricular restoration surgery. In patients with angina, PTCA or CABG is applied predominantly on the basis of symptoms and angiographic findings. If sternotomy can be avoided by employing PTCA in the potential transplant recipient, than so much the better. For patients with heart failure in the absence of limiting angina, early studies suggested that CABG was associated with poor short-term outcome and a perioperative mortality rate of 10–20%. Revascularization does not improve the function of scar tissue and it is impossible on the basis of echocardiography, coronary angiography, or ventriculography to determine which areas of the myocardium might benefit from improved perfusion.

An indication that segmental and global left ventricular function will improve after revascularization is obtained using imaging methods that provide evidence of myocardial viability. The techniques with the greatest evidence base for predicting recovery are those that provide confirmation of preserved metabolic activity, cell membrane integrity, or contractile reserve in dysfunctional regions. Positron emission tomography (PET), single photon emission tomography (SPECT) with Thallium-210 or Technetium-99m perfusion tracers, and low-dose dobutamine stress echocardiography have emerged as accurate and accepted methods for viability assessment, particularly when taken in combination.[18] Contrast-enhanced MRI also holds great promise in this area by providing very accurate information about left ventricular volume indices, myocardial wall thickness, and valve function.[19] Patients who benefit from viability testing include those with suspected coronary disease or dilated cardiomyopathy who are being considered for cardiac transplantation, and those with coronary disease and LV dysfunction (LVEF $< 35\%$) who are asymptomatic or have breathlessness with only mild angina. Viability testing is redundant in patients with unstable angina, postinfarction angina, and severe chronic stable angina because revascularization is indicated for symptomatic relief. For ischemic heart failure patients without angina, the combination of good target vessels and $> 25\%$ myocardial viability suggests the potential to benefit from CABG. For those with $< 25\%$ viability, poor target vessels, or in reoperative candidates, surgery is unlikely to produce improvement.[20] Other unfavorable patient characteristic include advanced age, female gender, severity of coronary artery disease, presence of preoperative dysrrhythmias, and renal failure. Table 4.2 provides guidelines supporting the use of CABG in preference to cardiac transplantation in patients with advanced ischemic cardiomyopathy.

DropBooks

TABLE 4.2. Guidelines for the use of CABG in preference to Cardiac Transplantation in patients with ischemic cardiomyopathy.

Condition	Intervention
Reversible ischemia LVESVI of < 60 ml/nr	CABG alone
Full-thickness scar and left ventricular aneurysm	Linear resection ± CABG
Akineric/dyskinetic left ventricle LVESVI of > 60 ml/m^2 with reversible ischemia	CABG + LV restoration surgery
Class III/IV mitral regurgitation	Mitral repair ± CABG
No reversible ischemia LVESVI > 100 ml/m^2	Left ventricular assist device or transplantation (no conservative option)
Pulmonary hypertension (PAP > 70 mmHg) Right ventricular failure	

LVESVI left ventricular end-systolic volume index (normal is <30 ml/m^2), *CABG* coronary artery bypass grafting, *PAP* pulmonary artery pressure.
Adapted from Hausmann et al.[27]

4.4.3. The Role of Left Ventricular Restoration Therapy

Ventricular restoration surgery is the successor to left ventricular aneurysmectomy, now that thrombolysis often arrests myocardial infarction before it reaches the transmural stage. Substantial improvement in left ventricular systolic function is uncommon after reperfusion therapy alone. With healing of infarcted myocardium, scar is maximal in the subendocardial region, though the epicardial surface may appear normal because of a rim of reperfused muscle. This contrasts with the leather-like appearance of full-thickness myocardial scar in a dyskinetic left ventricular aneurysm. MRI studies by Bogaert et al. demonstrated epicardial viability but loss of between 80% and 90% of contractile muscle in the endocardium and mid-myocardium after thrombolysis.[21] The veneer of epicardial salvage is not sufficient to prevent dilatation of the ischemic segment and increased sphericity. When more than 40% of the LV circumference becomes nonfunctional, the normal left ventricular end-systolic diameter index (LVESDI) of 25 ml/m^2 increases to > 60 ml/m^2. This is a threshold likely to be associated with subsequent cardiac mortality.

As LV size increases, the progressive LV hypertrophy and systolic wall stress account for worsening symptoms in ischemic patients. Stroke volume and global LV function gradually decline as ischemia progresses in the nonaneurysmal portion. Once decompensation begins, functional deterioration occurs rapidly with an increase in the risk of surgical mortality. For this reason LV restoration surgery should be considered in patients with an LVEF of <30%, mean pulmonary artery pressure of >25 mmHg, left ventricular akinesia or dyskinesia of >60%, and left ventricular end-diastolic volume (LVEDV) of >250 ml (LVEDV index >140 ml/m^2). Most of these patients are already NYHA III or IV with medical treatment.

Traditional left ventricular aneurysmectomy improved left ventricular function and heart failure symptoms by lowering LV wall stress. This linear amputation of a discrete dyskinetic scar commonly deformed the LV cavity into a box-like shape. Cooley and Jatene decreased surgical mortality by introducing intracavity patch reconstruction techniques to recreate an elliptical shape.[22,23] Dor further refined these methods and translated the application from well-defined dyskinetic scar to akinetic myocardial segments with normal epicardium.[24] At operation, the epicardium of the infarcted zone may appear normal, but the endocardial scar prevents wall motion improvements with revascularization alone.

Details of the Dor procedure are presented elsewhere. The overall effect is to reduce LV chamber size, restore the natural elliptical LV shape, and globally decrease wall stress (Figure 4.2). This also enhances function in myocardial regions remote from the repair. The operation is usually supplemented by surgical revascularization of suitable target vessels and mitral valve repair when necessary. Grades 3 and 4 mitral regurgitation is best addressed by standard mitral annuloplasty techniques. Grade 2 mitral regurgitation can be treated satisfactorily using the Alfieri stitch via the left ventriculotomy[25] (Figure 4.3).

4.4.4. Mitral Valve Repair in Ischemic Cardiomyopathy

There are now a number of clinical situations where mitral valve repair with or without revascularization improves the outlook for heart failure patients. These include the following:

1. Ischemia manifest by angina and variable mitral regurgitation, which become significantly worse

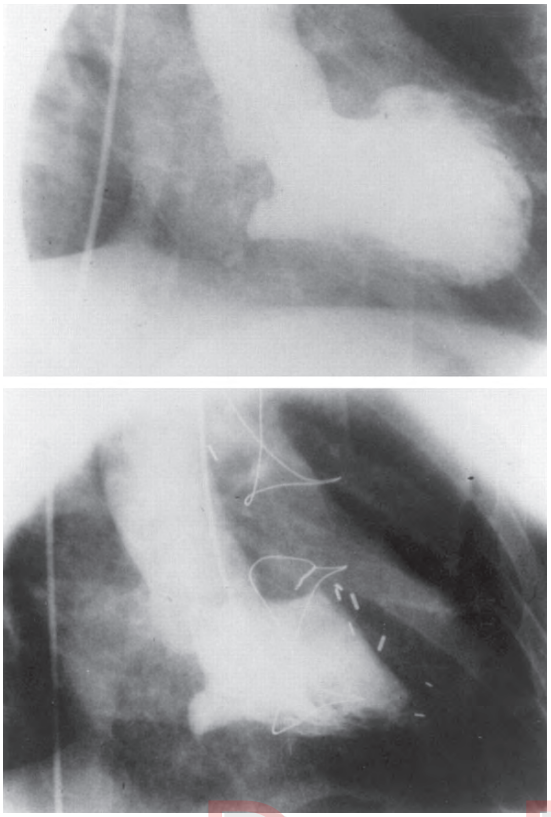


FIGURE 4.2. Left ventricular restoration surgery in an extreme case with very low ejection fraction and large left ventricular end-systolic volume. Before and after ventricular volumes and ejection fraction are shown.

during an acute ischemic episode, causing dyspnea at rest or left ventricular failure with pulmonary edema.
2. Acute myocardial ischemia or infarction located inferobasily (right coronary or dominant circumflex distribution) which causes sudden posteromedial papillary muscle dysfunction and mitral regurgitation.
3. Acute catastrophic pulmonary edema caused by papillary muscle rupture (inferobasal in 75% of the cases) several days after acute myocardial infarction.
4. Chronic progressive dyspnea (NYHA III or IV) associated with previous myocardial infarction, and enlarged dysfunctional left ventricle and various degrees of pulmonary hypertension. This comprises the largest group.

The recommended threshold for mitral repair in ischemic regurgitation is an LVESVI of >18 ml/m^2 or a calculated regurgitant fraction of >50% of the forward LVEF. Patients with angina, good target vessels, mild-to-moderate mitral regurgitation, and reversible ischemia posterolaterally on the PET scan can be treated by revascularization alone. Should valve replacement prove necessary, as much of the subvalvular apparatus as possible should be conserved to maintain left ventricular geometry and function. Division of all chordae tendonae is accompanied by a 47% reduction in LVE_{max} and a very deleterious effect on LV function (Figure 4.4).

DropBooks

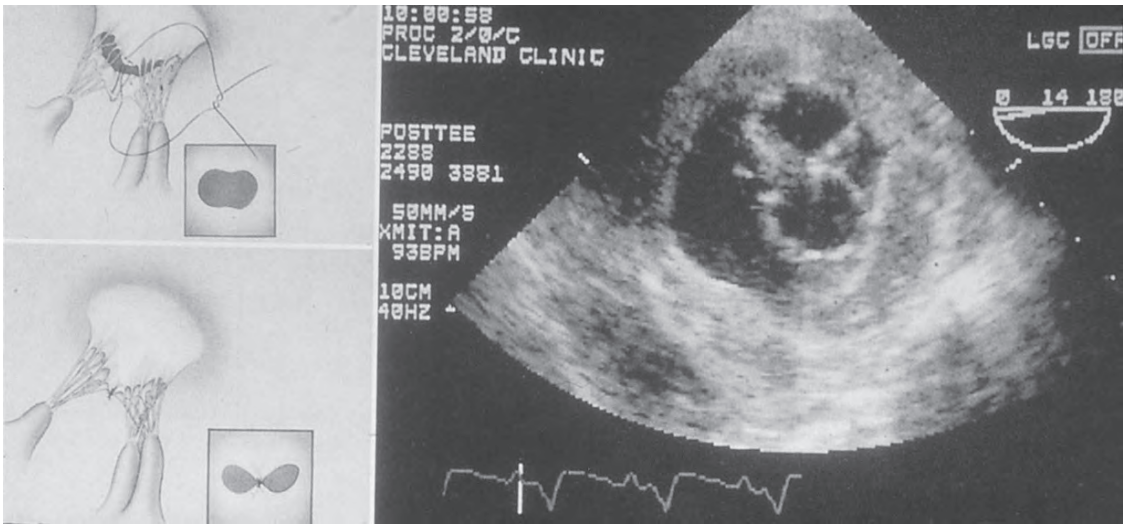


FIGURE 4.3. The Alfieri stitch joins the anterior and posterior mitral leaflets. This prevents anterior leaflet prolapse and produces a two-channel orifice.

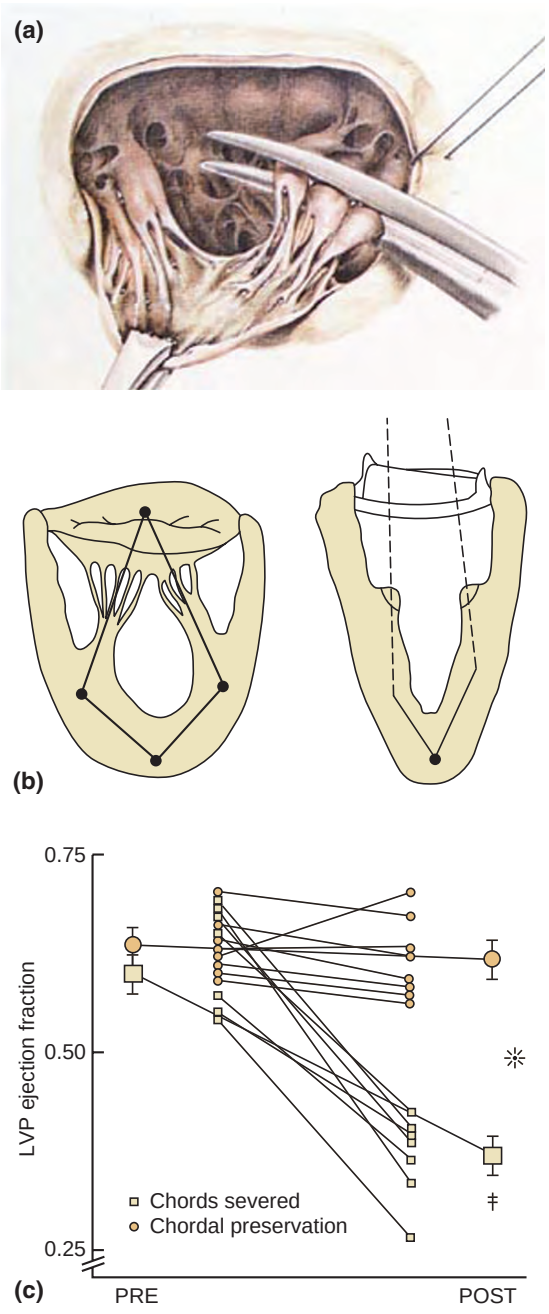


FIGURE 4.4. Negative effect of transecting the mitral subvalvular apparatus during mitral valve replacement.

Ischemic mitral regurgitation is a functional problem of unsuccessful coordination of the entire mitral apparatus rather than simple failure of a single papillary muscle. Mitral annuloplasty with significant undersizing of the valve ring greatly increases leaflet coaptation. Systolic anterior motion (SAM) is avoided because of widening of the aorto-mitral angle and increased left ventricular size. The undersized valve ring acutely remodels the base of the myopathic heart helping to reestablish an ellipsoid shape to the left ventricle.

Clearly, in many cases of ischemic cardiomyopathy, no conservative option is possible. These patients have advanced left ventricular remodeling with an LVESVI of >100 ml/m^2, suffer breathlessness with no angina, and have no reversible ischemia on viability testing. This combination is often associated with a degree of right ventricular failure and pulmonary hypertension with a right atrial pressure exceeding 20 mmHg. For these patients, cardiac transplantation or a "lifetime" left ventricular assist device (LVAD) implant are the only options. The role of cardiac transplantation will be considered later in this chapter. The potential for "lifetime" mechanical circulatory support has been tested in the Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH) trial and is even more promising with the introduction of the miniaturized continuous flow pumps.[26]

4.5. Outcome After Non Transplant Surgery for Ischemic Cardiomyopathy

Useful data regarding patients selection and outcome for high-risk revascularization have emerged from centers where transplant candidates were selected out for CABG instead. Hausmann et al. in Berlin compared 225 potential transplant candidates who underwent CABG with 231 others who received a donor organ.[27] This was not a randomized trial. Differences between the groups were the longer duration of symptoms, the presence of right heart failure, and a greater incidence of previous CABG in the heart transplant recipients. Operative risk in the CABG group was significantly higher for those with a greatly increased end-diastolic pressure (LVEDP >24 mmHg), a low preoperative cardiac output (<2.0 l/min/m^2), and for patients in NYHA IV. Hospital mortality was 7.1% for the CABG patients versus 18.2% in the transplant group. There was no significant difference in hospital mortality in patients with an LVEF between 10% and 20% versus those with an LVEF between 20% and 30%. Survival for the CABG

group was 78.9% after 6 years versus 68.9% for the transplant group. Reinvestigation of CABG patients showed a significant decrease in mean pulmonary artery pressure from 28.2 mmHg to 21.2 mmHg ($p < 0.01$). Pulmonary capillary wedge pressure fell from 19.2 mmHg to 13.1 mmHg ($p < 0.01$) and LV ejection fraction improved from a mean of 0.24 to 0.39 ($p < 0.0001$). Others have reported similar findings.[28]

Observational studies have documented substantial improvement in LV regional and global function following revascularization of hibernating myocardium.[29] Relief from heart failure symptoms, quality of life benefit, and improved survival have been demonstrated in these patients. The necessity for viability assessment in patient selection was demonstrated by Hass in a series of 69 patients with three-vessel disease and an LVEF of < 35%.[30] Thirty-five patients were operated on the basis of angiographic findings alone, whereas 34 were selected on the basis of PET-documented hibernating myocardium and favorable target vessels. The hibernating myocardium group had a lower hospital mortality (0% vs 11.4%, $p = 0.04$), a lower incidence of postoperative complications (33% vs 67%, $p = 0.05$), and fewer patients with low cardiac output syndrome (3% vs 17%, $p = 0.05$). Furthermore, the 1-year survival rate was better (97 ± 8% vs 79 ± 8%, $p < 0.01$). The LVEF increased from 26% to 35% ($p = 0.003$) in those with myocardial viability but was unchanged in those without. Similarly, in a retrospective review of 70 ischemic cardiomyopathy patients undergoing CABG, Pagley demonstrated a significantly improved short- and long-term cardiac event-free survival in patients with hibernating myocardium.[31] In those who were similar with regard to age, gender, presenting clinical syndrome, hemodynamical variables, number of diseased coronary arteries, and LVEF, the myocardial viability index was the only independent predictor of event-free survival. Tjan et al. compared the outcome in 51 potential transplant candidates (all LVEF < 20%) who underwent CABG instead, with 163 others who underwent transplantation.[28] The survival analysis was performed on the basis of intention to treat independent of subsequent transplantation. Groups were comparable with regard to LV function, pulmonary capillary wedge pressure, and serum creatinine. Patients in the CABG group were older (63 ± 8) and included a higher percentage of females. One-year survival was similar in both groups (CABG 71.9% vs transplant 66.3%). In CABG patients, hospital survival was 88.2%. Preoperative serum creatinine and the nonusage of the left internal thoracic artery were predictors of adverse outcome. The authors concluded that up to 50% of transplant candidates can be redirected toward CABG after assessing myocardial viability and general risk factors such as age, peripheral vascular disease, history of hypertension, and suitability of the target vessels. In contrast, selection according to preoperative LVEF was not useful. Only the degree of myocardial viability was predictive of outcome. The authors recommended preoperative insertion of an intra-aortic balloon pump and LVAD stand-by during the operation.

With worsening donor availability, many transplant centers now support the high-risk revascularization strategy as an alternative.

Although CABG may provide better short-term results than transplantation, the benefits may be time-limited. Luciani showed only 47% of patients with advanced preoperative left ventricular dysfunction to be free from heart failure symptoms 5 years after CABG, despite 75% survival at this time.[32] CABG appears to influence the mode of death, however. Mortality occurs predominantly through left ventricular failure and not dysrrhythmias, which otherwise accounts for more than 60% of deaths in unoperated ischemic cardiomyopathy.

DropBooks

4.5.1. The Variable Improvement in Myocardial Function

Irrespective of the symptomatic and survival benefits afforded by revascularization, the functional response is unpredictable. In detailed studies of regional perfusion, glucose usage, and contractile function, Bax et al. showed functional improvement in only 70% of stunned myocardial segments and 31% of hibernating segments by 3 months.[33] While there was no further improvement in stunned segments, 61% of hibernating segments manifest gradual improvement in wall motion score by 14 months. Haas studied the time course of functional recovery in relation to the histology (intraoperative biopsy) from dysfunctional areas.[34] PET was used to distinguish stunned from hibernating

myocardium. Stunning was identified in 70% of 240 dysfunctional segments and hibernation in 24%. Hibernation was associated with more severe depression of wall motion and incomplete postoperative recovery. One year after revascularization, only 31% of stunned segments and 18% of hibernating segments showed complete functional recovery. Failure to improve was associated with more severe degenerative ultrastructural changes in the myocyte. The authors concluded that myocardial stunning was more prevalent than hibernation and that myocardial morphology determined the time course and extent of functional improvement after revascularization.

The observation that only 31% of stunned myocardial segments attained complete functional recovery challenges the definition of "stunning" from which complete recovery is expected over time. In this population with severe long-lasting coronary artery disease, previous infarction, and a history of congestive heart failure, it is likely that other factors such as the degree of left ventricular remodeling and persistent elevated wall stress may preclude myocardial recovery. Myocardial histology in these patients suggests a continuum between stunning and hibernation with structural hibernation representing the limit of viability. Kim and colleagues, using enhanced contrast MRI, found that 78% of dysfunctional segments with full-thickness wall viability showed improvement in contractility after revascularization.[35] In contrast, 90% of the regions with 50–75% of wall thickness scar did not improve. These regions would be considered entirely nonviable according to echocardiographic wall motion criteria, even though a substantial epicardial rim of viable tissue remains. Maes showed the degree of fibrosis within the myocardial segment to be a determinant of improvement.[36] Others have shown severely hypokinetic or akinetic segments to have a 2.4-fold increase in α-receptor density with a concomitant 50% decrease in β-receptor density compared with normal segments.[37] Graded reciprocal changes in α-and β-adrenergic receptor density in hibernating myocardium may account in part for the depression in resting myocardial function, and confirms that alterations in β-receptor density are associated with hibernating myocardium. These observations must be kept in mind when considering nontransplant surgical options. Risk of mortality must be balanced against the likelihood of symptomatic benefit.

In contrast to the somewhat slow and unpredictable recovery after CABG, left ventricular restoration surgery produces an immediate result. Dor studied a cohort of 781 ventricular restoration patients (age 57 ± 7 years) with mean LVEF 17 ± 3%.[38] All were NYHA class III or IV before surgery. Hospital mortality was 19.3% but ejection fraction improved from 17 ± 3% to 37 ± 10% ($p < 0.0001$). By multivariate analysis, factors that influenced early mortality were the presence of critical narrowing in the circumflex coronary artery and the duration of cardiopulmonary bypass. At 1-year follow-up, a significant improvement in NYHA class was observed with no patients remaining in NYHA IV. Improvement in LVEF was maintained (39 ± 11%) as well as the reduction in inducible and spontaneous ventricular tachycardia. Late mortality was 10% at 5 years. Buckberg et al. applied left ventricular restoration to a series of elderly patients (mean age 77 years, all NYHA class IV) with a history of multiple admissions for congestive heart failure and gross LV enlargement.[39] Preoperatively, the mean LVEF was 20% (±8.5%), LVEDV was 300 ± 105 ml, and LVESV was 243 ± 81ml (LVEDV index 169 ± 55 ml/m^2 and LVESVI 132 ± 41 ml/m^2). After surgery LVEF increased from 20% to 35%. The average LVEDV was reduced by 80 ml (from 300 ml to 220 ml), an average of 28%. LVESV was reduced from 243 ml to 149 ml, an average of 49%. LVEDV index was reduced by 48 ml/m^2 (from 170 ml to 121 ml/m^2) and the LVESV index was reduced 45 ml/m^2 (from 132 ml to 81 ml/m^2).

An additional benefit of volume reduction may be the shape alteration that realigns muscle fibers' orientation to allow optimal ejection. Spotnitz has described transmural shearing planes on cross-sections of the myocardium.[40] Contractile fibers run perpendicular to these planes and thickening of contracting heart muscle is produced by torsion or deformation of these fibers. This change in myocardial thickening is responsible for LV ejection and is evident during MRI of the LV wall. The torsion is related to the angle of fiber orientation with a conical formation toward the apex. The Dor procedure restores elliptical fibers orientation and improves wall thickening during LV contraction. Shape restoration produces a more normal

orientation of the sinobulbar and circular muscle around the LV and reestablishes an ellipsoid form to improve systolic twisting compression.

In 1998, Buckberg and Dor initiated an international cooperative study to investigate the results of surgical LV restoration on a multicenter basis.[41] Nine centers reported on 449 patients with mean age 63 ± 10 years with a baseline LVEF of 28% ± 10% and median LVESVI of 110 ml/m^2. Anterolateral akinesia was present in 67% and LV aneurysm (dyskinesia) in 33%. Ninety-six percent of the patients had CABG and 23% had mitral valve repair. Only 7% required intra-aortic balloon pump support. Hospital mortality rate was 5.7%, estimated 1.5-year mortality rate was 10%, and rehospitalization rate for congestive heart failure was 5%. LVEF increased to 39% ± 12.6% (an increase of 10.5%) with a median LVESVI of 68 ml/m^2 (a 35.4 ml/m^2 decrease). The 88% late survival for those who underwent LV restoration and CABG suggest that this strategy is safe and at least equivalent to CABG alone. Whether LV restoration added to CABG improves outcome can only be answered by a randomized trial of these surgical options (as currently underway in the surgical treatment for ischemic heart failure (STITCH) trial).

Neither previous coronary surgery nor ventricular restoration preclude cardiac transplantation though long-standing ischemic patients frequently have comorbidities (diabetes; chronic obstructive pulmonary disease, COPD; renal impairment; or right heart failure) to preclude this option.

4.5.2. The Potential Role of Stem Cell Therapy

Collectively, these studies suggest that, when ischemic cardiomyopathy patients are sufficiently stable to undergo elective surgery, repair is better than replacement. This policy may soon be reinforced by the introduction of autologous stem cell therapy whereby bone marrow stem cells are harvested from the iliac crest at the beginning of an open operation, processed in the laboratory, and then injected directly into ischemic myocardium during coronary bypass surgery.[42] Alternatively, catheter-based delivery can be applied through the endocardium using an electromechanical mapping (EMM) system.[43] This locates ischemic but viable myocardium and allows the injection catheter to be directed to the intraventricular target site. Around 30 million stem cells are introduced with the aim of inducing vasculogenesis and possibly generating new cardiac myocytes. The Texas Heart Institute have performed more than 500 such procedures with an excellent safety record and clinical benefit including objective evidence of enhanced myocardial perfusion, improved LVEF, and longer treadmill exercise performance. Autologous bone marrow stem cells have not provided the same risk of dysrrhythmic events as autologous myoblast implants and have no contentious ethical issues as for embryonic stem cells. Although it is unclear whether the stem cells create new vascular or cardiac muscle cells, or stimulate the development of one of both types of cells, the treatment protocol has proven to be sufficiently safe and effective to allow the Food and Drug Administration (USA) to approve a randomized clinical trial.

4.6. Which Patients Should be Transplanted?

Cardiac transplantation is an irreversible operation. The survival and symptomatic benefits were reported by the Stanford group in 1976 and have only recently been subjected to critical analysis in the light of improved medical and nontransplant heart failure surgery.[44] The identification of heart transplant candidates is based on the expected gain in survival and quality of life when compared with organ-conserving therapeutic options.[45] There have been no prospective randomized trials. Hospital survival has improved from around 75% in the early 1980s to 85% by 2000. Ten-year survival is around 50%.[46] In parallel with improved outcome for transplantation, medical management by specialist heart failure cardiologists has reduced heart failure mortality. Between 1990 and 2000, the waiting list mortality for patients receiving an LVAD or intravenous inotropes (Status 1) decreased by 63% and by 55% for outpatients waiting at home in a stabile condition (Status 2). In fact, the United Network for Organ Sharing identifies the fact that 1-year mortality for Status 2 patients approximates to 1-year survival after transplantation (87% ± 1%), revealing no definite survival advantage for Status 2 transplant candidates.[1] Between 1990 and 1999, the waiting list death rate fell from 432.2/1,000 patient/years to 172.4/1,000 patient/years. Clearly,

DropBooks

mortality rate varies with risk status. For Status 1a patients with profound hemodynamic instability requiring LVAD support or high-dose intravenous inotropes, the waiting list mortality remains at 589 deaths/1,000 patient/years. This contrasts with 204.7 deaths/1,000 patients/year for Status 1b patients on low-dose intravenous inotropes and 130.7 deaths/1,000 patients/year for Status 2 patients.

The German Transplant Society and Eurotransplant International Foundation studied all 899 adult patients listed for cardiac transplantation in Germany in 1997. In the Comparative Outcomes and Clinical Profiles In Transplantation (COCPIT) study, the patients were stratified into high-, medium-, and low-risk categories according to the Heart Failure Survival Score.[47] Waiting list mortality was 32% in high-risk patients and 20% in each of the medium and low-risk groups. Controversially, by 18 months after transplantation a clear survival advantage could only be shown in the group with the highest risk of waiting list mortality. To refine risk stratification in ambulatory patients (Status 2), the University of Pennsylvania and the Colombia University, New York, independently validated prognostication based on the Heart Failure Survival Score.[48] At 1 year, survival for high-risk patients was 43 ± 7%, medium-risk 72 ± 5, and low-risk 93 ± 2%. This shows that the event-free survival for high- and medium-risk waiting list patients was much worse than after transplantation, whereas for the low-risk patient survival was better than after transplantation. Accordingly, Deng's report suggest that with modern medical management (including cardiac resynchronization therapy and implantable defibrillators), the outlook for many stable non–inotrope-dependent Stage D patients is better without transplantation.

Clearly, the very restricted number of donor organs should be reserved for those patients most likely to benefit in life expectancy and quality of life. Absolute indications for transplantation include refractory cardiogenic shock, dependence on intravenous inotropic support (both Status 1), or persistent class IV symptoms with peak oxygen consumption (MVo_2) <10 ml/kg/min. Hemodynamic or renal indications to discontinue angiotensin-converting enzyme (ACE) inhibitors and intolerance of β-blockade reinforce the need for transplantation in Status 2 patients. In the high-risk category above, benefit is the difference between a 1-year survival of less than 50% versus 83% after a transplant. In practice most patients awaiting transplantation are ambulatory (Status 2), on oral medication with an MVo_2 between 11 and 14 ml/kg/min. Many of these patients improve symptomatically and prognostically during follow-up by the transplant center. The likelihood of improvement is increased by selection of less ill patients (by excluding those with renal impairment and comorbidities). As many as 30% of Status 2 candidates can be removed from the waiting list with excellent early survival. Shah et al. showed that survival at 1 and 3 years for Status 2 patients removed from the transplant waiting list after 6 months of optimized treatment was 100% and 92%, respectively.[49] Patients with idiopathic dilated cardiomyopathy had better outcomes than those with ischemic cardiomyopathy. Accordingly, patients are deemed too well for transplantation if they are clinically stabile with the sustained improvement of MVo_2 by >2 ml/kg/min. There is therefore a need for repeated reevaluation of Status 2 candidates by measurement of MVo_2.

Given the improved short-term survival of many Stage D heart failure patients, there are continuous efforts to define which patient will gain maximum long-term benefit from a donor heart. With the lack of secure information regarding risk-adjusted (patient-specific) time-related survival estimates for different etiologies of heart failure, uniform agreement has not been achieved among transplant centers regarding the precise indications and timing of transplantation. Survival benefit margin is assessed by calculating the patient's specific survival probability with transplantation minus the survival expectation without transplantation during the same time period. For instance, a patient with only 60% expected 1-year survival after transplant but with a 20% expected 1-year survival without would have a survival benefit margin of 40% in 1 year. In contrast, a patient with stable advanced heart failure may have a projected 1-year survival of 70% on medical therapy compared with 90% with transplantation. Such a patient would have a lower survival benefit margin (20%) but an improved use of the donor heart in terms of expected graft and patient survival. Currently, allocation of donor organs

is governed by two axioms that are sometimes contradictory: equity (equal access of all patients to donor organs) with priority given to patients closest to death; and utility (an allocation policy for organ that maximizes patient and graft survival). Application of these principles requires that a lower limit of acceptable expected post-transplant survival be determined, and that secure patient-specific information about mid-term survival with medical therapy for subsets of advanced heart failure is available. Irrespective of survival, the short- and long-term quality of life/benefit is more difficult to quantify and is dependent upon the condition of other organ systems, which have been affected by the severity and chronicity of heart failure. Therefore, an important component of transplant evaluation is the assessment of comorbid conditions that independently reduce duration or quality of life.

In a study by Kirklin et al. from the Cardiac Transplant Research Database (CTRD) of 7,283 patients from 42 North American institutions (over 24,000 years of follow-up), patients with multiple comorbid conditions were shown to have significantly worse intermediate-term survival than those without comorbidity.[50] Patients were stratified low-risk when under the age of 65 with no other risk factors (insulin-dependent diabetes, peripheral vascular disease, COPD, smoking within 6 months, gender mismatch, or congenital etiology). A donor age <40 years and ischemic time <240 min were associated with a low risk of complications. On the other hand, patients with significant comorbidity, particularly those on a ventilator at the time of transplant and with a donor age >56 years or ischemic time >360 min had much less satisfactory outcomes. Whereas patients categorized as low risk had 89% survival at 1 year and 80% 2-year survival, the corresponding figures for the high-risk group were 71% and 58%.

General guidelines for transplant wait-listing are shown in Table 4.3. In practice, it is easier to define contraindications to transplantation (Table 4.4). Alhough age restriction is difficult to justify except on the ground of donor organ availability, Frazier (personal communication) has shown that transplantation provides very effective treatment for ischemic cardiomyopathy patients in their 70s..

Table 4.3. General indications for cardiac transplantation.

Criteria for consideration of heart transplantation in *advanced heart failure*
Significant functional limitation (NYHA class III–IV heart failure) despite maximum medical therapy that includes digitalis, diuretics, and vasodilators, preferably angiotensin-converting enzyme inhibitors, at maximum tolerated doses.
Refractory angina or refractory life-threatening arrhythmia
Exclusion of all surgical alternatives to transplantation, such as the following:
Revascularization for significant reversible ischemia
Valve replacement for severe aortic valve disease
Valve replacement or repair for severe mitral regurgitation
Appropriate ventricular remodeling procedures
Indications for cardiac transplantation determined by severity of heart failure despite optimal therapy
Definite indications
VO_{2max} < 10 ml/kg/min
NYHA class IV
History of recurrent hospitalization for congestive heart failure
Refractory ischemia with inoperable coronary artery disease and left ventricular ejection fraction of < 20%
Recurrent symptomatic ventricular arrhythmias
Probable indications
VO_{2max} < 14 mg/kg/min (or higher with multiple other risk factors)
NYHA class III–IV
Recent hospitalizations for congestive heart failure
Unstable angina not amenable to coronary artery bypass grafting, percutaneous transluminal coronary angioplasty with left ventricular ejection fraction of < 0.25%

Table 4.4. Contraindications to cardiac transplantation.

General contraindications
Presence of any noncardiac condition that would itself shorten life expectancy or increase the risk of death from rejection or complications of immunosuppression
Specific contraindications [a]
Age greater than about 65 years (program variability)
Active infection
Active ulcer disease
Severe diabetes mellitus with end-organ damage
Severe peripheral vascular or cerebrovascular disease
Coexisting neoplasm
Morbid obesity
Creatinine clearance of <40–50 ml/min, effective renal plasma flow (ERPF) of <200 ml/min [b]
Bilirubin >2.5 mg/dl, transaminases >2× normal [c]
Severe pulmonary dysfunction with forced vital capacity (FVC) and forced expiratory volume in the 1st sec (FEVI) of <about 40% of predicted, especially with intrinsic lung disease
Pulmonary artery systolic pressure of >60 mmHg, mean transpulmonary gradient of >15 mmHg, or pulmonary vascular resistance of >5 Wood units [d]
Acute pulmonary thromboembolism
Active diverticulitis
High risk of life-threatening noncompliance

(continued)

DropBooks

Table 4.4. (continued)

Inability to make strong commitment to transplantation
Cognitive impairment severe enough to limit comprehension of medical regimen
Psychiatric instability severe enough to jeopardize incentive for adherence to medical regimen
History of recent smoking (within 6 months)
History of recurring alcohol or drug abuse
Failure of established stable address or telephone number
Previous demonstration of repeated noncompliance with medication or follow-up
Lack of independent family or social support system
History of marked depression or emotional instability

[a]May be relative or absolute depending on severity or program philosophy.
[b]May be suitable for cardiac transplantation if inotropic support and hemodynamic management produce a creatinine level of < 2 mg% and creatinine clearance of > 50 ml/min. Transplantation may also be advisable as combined heart kidney transplant.
[c]Requires liver biopsy to exclude cirrhosis or other intrinsic liver diseases.
[d]These apply only if the increased resistance is largely nonreactive *(fixed)*.

4.7. Lifetime Mechanical Circulatory Support

As it becomes socially less acceptable to discard patients at 65 years, indefinite mechanical circulatory support now provides an important off-the-shelf alternative therapy with the potential to exceed transplant numbers by a factor of 50 to 1.

While the evidence base for transplantation in non–inotrope- or device-dependent patients become less secure, the use of mechanical circulatory support as an alternative to maximum medical therapy has a strong evidence base in the REMATCH trial.[26] There are important differences between the application of mechanical cardiac support for acute circulatory failure versus chronic cardiac deterioration. Blood pumps implanted electively for chronic cardiomyopathy are usually placed in patients with long-standing heart failure who remain severely symptomatic or decompensate on maximum medical therapy. In general, the end organs have been subjected to prolonged periods of low cardiac output and have adapted to this over time. Under these conditions, the majority of patients are well served with implantable LVAD alone. Even in the presence of high pulmonary vascular resistance, the right ventricle rarely needs support (no more than 10% of patients).[51] On the other hand, patients with acute cardiogenic shock after massive myocardial infarction without preexisting cardiomyopathy are subjected to profound low-flow states, which cause multiple organ failure if not promptly reversed. Under these circumstances, biventricular support is particularly valuable and in extreme cases biventricular replacement with the CardioWest total artificial heart may be required to sustain life in potential transplant candidates[52] (Figure 4.5).

4.8. Decision-Making in Patients with Idiopathic Dilated Cardiomyopathy

The natural history of idiopathic dilated cardiomyopathy is less predictable than for ischemic cardiomyopathy. Remission and prolonged survival are well documented in transplant-listed Stage D patients. In Shah's analysis of survival in patients removed from a heart transplant waiting list, freedom from death 8 years after wait-listing exceeded 80% for idiopathic dilated cardiomyopathy, compared with around 30% for ischemic patients.[50] In addition to improvement on medical management, left ventricular unloading with an LVAD has the propensity to provide sustainable recovery in myocardial function in selected patients.[53] With increasing awareness of the mechanisms of ventricular recovery, together with the availability of other nontransplant surgical options, it is debatable whether cardiac transplantation should be undertaken as the primary treatment for this condition.

In dilated cardiomyopathy the projected mortality is directly related to the severity of systolic dysfunction. Increased chamber sphericity and the presence of mitral regurgitation are markers of worse prognosis (1-year mortality 54–70%). As the failing left ventricle dilates, the papillary muscles are displaced, coaptation of the mitral valve leaflets is decreased, and a central jet of mitral regurgitation appears (Figure 4.6). Mitral regurgitation then leads to more volume overload of the already dilated chamber.

4.8.1. Mitral Valve Repair

Reports of prohibitive operative mortality for mitral valve replacement in dilated cardiomyopathy patients in the early 1980s implied that the failing



Figure 4.5. Patient with the CardioWest total artificial heart awaiting cardiac transplantation as an outpatient. (Courtesy of Drs. A. Banyosy and R. Korfer).

DropBooks

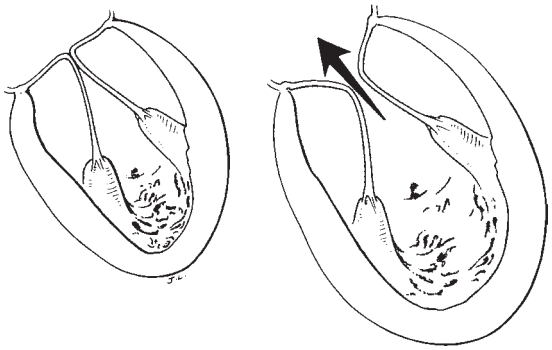


FIGURE 4.6. The mechanism of mitral regurgitation in idiopathic dilated cardiomyopathy.

ventricle will deteriorate further if the "blow-off" into the left atrium is removed. More recent information shows that mitral valve repair with preservation of the subvalvular apparatus carries low perioperative mortality, good medium-term survival, and symptomatic relief through improvement in cardiac index. Bolling has reported the effects of mitral repair in patients with very advanced disease.[53] All had severe left ventricular systolic dysfunction with preoperative LVEF ranging from 8% to 25% (mean 16 ± 3%). The average duration of cardiomyopathy was 4 years (range 0–16). All patients underwent remodeling ring annuloplasty with an undersized flexible ring and half had tricuspid annuloplasty. Hospital mortality was less than 2% while 12- and 24-month survival were 82% and 72%, respectively. All patients were restored to NYHA class I or II with a mean postoperative LVEF of 26%. Peak MVO_{2max} rose from a mean of 14.5 to 18.6 ml/kg/min. Echocardiography at 2 years postoperatively showed a pronounced reduction in sphericity, regurgitant volume, and regurgitant fraction. LVEF and end-diastolic and end-systolic volumes were all improved (Table 4.5). Others have not achieved the same degree of success with this approach.

TABLE 4.5. Change in ventricular function and size after mitral repair in patients with advanced heart failure.

Variable	Preoperative	Postoperative	Change (%)[a]	*p* Value
End-diastolic volume (ml)	335 ± 107	307 ± 103	−8 ± 9	0.06
End-systolic Volume (ml)	277 ± 101	237 ± 98	−15 ± 14	0.03
Stroke volume (ml)	58 ± 13	70 ± 21	12 ± 10	0.02
Ejection fraction (%)	18 ± 5	24 ± 10	31 ± 24	0.03
Mitral inflow (l/mm)	12.4 ± 5.3	5.4 ± 0.5	−49 ± 22	0.02
Forward cardiac output (l/min)	3.2 ± 1.0	4.7 ± 0.9	52 ± 38	0.01
Regurgitant volume (l/min)	9.2 ± 5.4	0.8 ± 0.6	88.6 ± 10.1	0.01
Regurgitant fraction (%)	70 ± 14	15 ± 11	−79 ± 15	<0.001

[a]Percentage change from preoperative study at 4–6 months postoperatively. The NYHA class fell significantly from 3.9 ± 0.4 to 1.8 ± 0.5 (*p* Value <0.001).
From Bolling et al.[53]
© 2007 by The American Association for Thoracic Surgery.

4.8.2. External Cardiac Constraint

Following the disappointing results of dynamic skeletal muscle cardiomyoplasty, a much simpler concept has evolved to prevent the progression of left ventricular remodeling in dilated cardiomyopathy. Acorn Cardiovascular (Saint Paul, Minnesota) developed a passive constraint device of mesh-like polyester material to surround the left and right ventricle[54] (Figure 4.7). The fabric has a unique bidirectional compliance that allows the mesh to conform to the ellipsoid surface of the heart. The passive jacket is positioned around the ventricles and sutured posteriorly and laterally, slightly above or below the atrioventricular groove. This provides a slight and immediate reduction in the circumference of the heart. Animal models suggest a reduction in left ventricular volume and improved cardiac function compared with controls.[55] Obviously, the mesh does not improve cardiac contraction, but it appears to prevent further deterioration. So far there is no evidence of constrictive physiology; the normal response to volume loading is preserved, left and right heart filling pressure do not equalize, and transmitral flow parameters do not change significantly. Myocardial biopsies from the animal models suggest a degree of reverse remodeling with the tendency toward less myocyte hypertrophy, less interstitial fibrosis, and higher capillary density in the treated animals.

In clinical studies, application has been restricted to NYHA class II or III patients, many of whom were also subject to mitral valve repair or replacement or left ventricular restoration surgery. The Acorn device did not significantly improve left ventricular end-diastolic dimensions, LVESV, peak oxygen consumption, or degree of mitral regurgitation when used in isolation. The safety and feasibility studies confirm that the device does not cause constrictive or restrictive physiology, has no effect on the epicardial coronary vessels, and can prevent progressive remodeling. In contrast, the effects

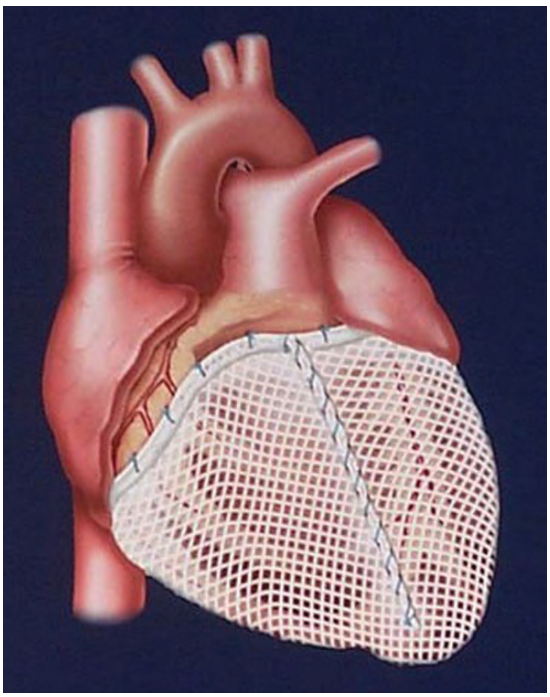


FIGURE 4.7. The Acorn external constraint device.

on LVEF and cardiac output (independent from concomitant procedures) are limited. Important questions remain with regard to patient selection, potential long-term adverse effects, and the optimal timing for ventricular restraint. However, it is possible that early ventricular compressive therapy after myocardial infarction could dramatically ameliorate the remodeling process. Whether external restraint will remain in the surgical armamentarium for dilated cardiomyopathy remains to be seen.

4.8.3. Partial Left Ventriculectomy (Batista Operation)

The importance of wall stress and the LaPlace principle is axiomatic in Batista's partial left ventriculectomy operation (Figure 4.8). The concept that a dilated heart with thinned walls functions poorly because the myocytes are placed at a mechanical disadvantage was addressed by attempting to restore "normal" left ventricular geometry with reduced wall stress and improved contractile function.[56] This relies on an assumption that noninfarcted (but diseased) myocardium can contract normally if wall stress is reduced. The concept completely ignores the cellular and molecular changes in the failing heart, which account for the disappointing early and late results of this operation. Despite this, partial left ventriculectomy was widely adopted as an alternative to transplantation without guidelines or convincing information about sustainability and survival. The published hospital mortality was prohibitive, ranging from 1.8% to 27% with an average of 17.4%.[57] Acceptable hospital mortality was achieved by some centers with the aid of long-term LVAD support (20% of patients) and cardiac transplantation. In survivors, an immediate significant decrease in both end-diastolic and end-systolic volume indices was achieved. While LVEF improved initially, some restudies at 12 months failed to show significant differences from preoperative LVEF in many patients.

The suggested mechanism for initial improvement in LVEF was a reduction in systolic wall stress rather than a change in contractility. There was an inverse relationship between the decrease of circumferential end-systolic stress and increase in LVEF. In McCarthy's series, mean LVEF improved from 13% to 21% and peak oxygen consumption from 11 ml/kg/min to 16 ml/kg/min at 12 months.[57] Twelve-month survival at the Cleveland Clinic was 80% but LVADs were required for bridge-to-transplantation in 16% of patients. Freedom from heart failure of any cause (including relisting for

DropBooks

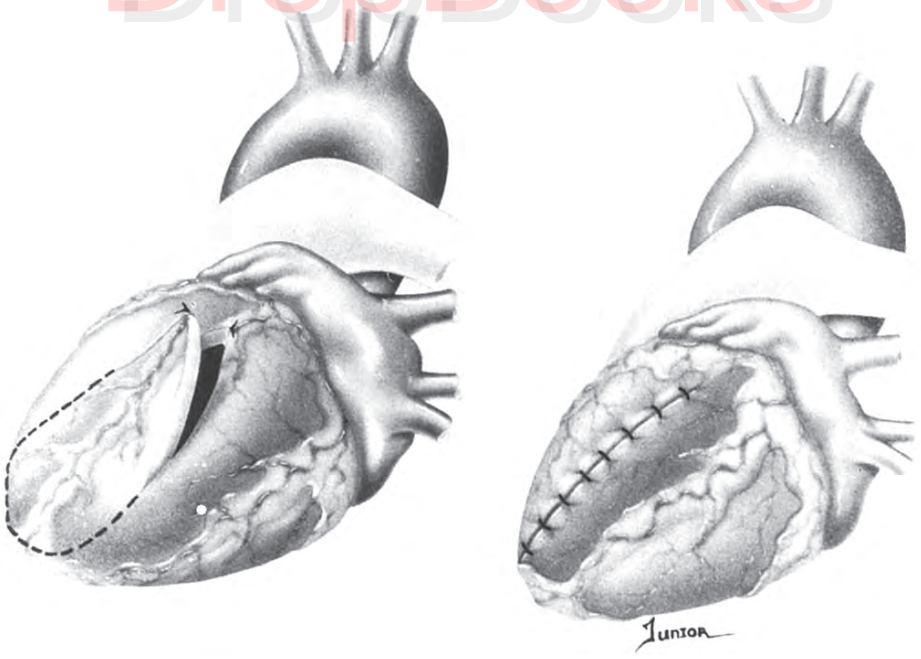
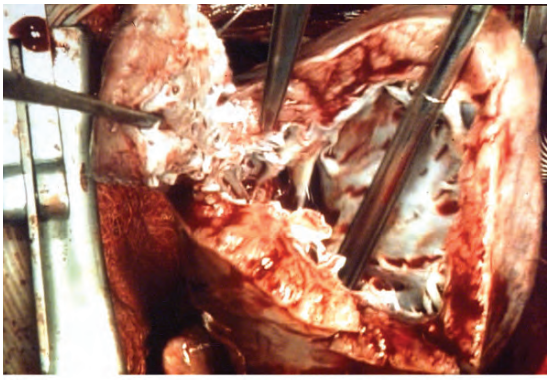


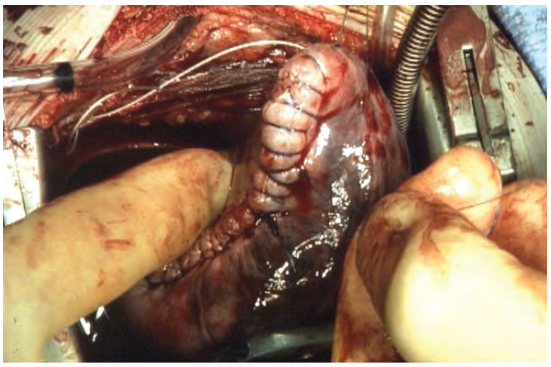
FIGURE 4.8. The "Batista" partial left ventriculactomy operation.

transplant, death, or class IV symptoms) was only 50% by 12 months and 38% at 2 years. Alhough the reduced ventricular geometric dimensions may be sustained up to 12 months, pump function began to deteriorate after 6 months. The discrepancy between geometry and sustainability of mechanical function was attributed to the fact that left ventricular mass reduction caused changes in diastolic compliance.

Currently, most centers that considered partial left ventriculectomy as a promising alternative to transplantation have redirected this procedure to a small number of highly selected dilated cardiomyopathy patients. With emerging alternatives, the Batista operation has joined skeletal muscle cardiomyoplasty in the dustbin of heart failure operations. Even so, the author has some remarkably successful long-term outcomes in very sick infants without alternatives (Figure 4.9).



a



b

FIGURE 4.9. Partial left ventriculectomy in an infant with anomalous left coronary artery from the pulmonary artery and endocardial fibrosis who could not be weaned from cardiopulmonary bypass after the repair. Ventricular remodeling improved cardiac function and she is NYHA I 5 years later.

4.8.4. Mechanical Unloading in Dilated Cardiomyopathy

The propensity for the idiopathic dilated cardiomyopathy heart to improve with a combination of ACE inhibitors and β-blockade reflect the beneficial properties of preload and afterload reduction with reduced wall stress. This therapeutic effect on the remodeling process can be greatly amplified by mechanical unloading with an LVAD. The LVAD functions in series with and completely offloads the native LV so that the aortic valve remains closed (Figure 4.10). The improved systemic blood flow improves coronary blood flow, gradually reverses multiorgan failure, and increases physical activity. Serum aldosterone, plasma renin, atrial natriuretic peptide, and norepinephrine levels revert to normal as the heart failure syndrome disappears.

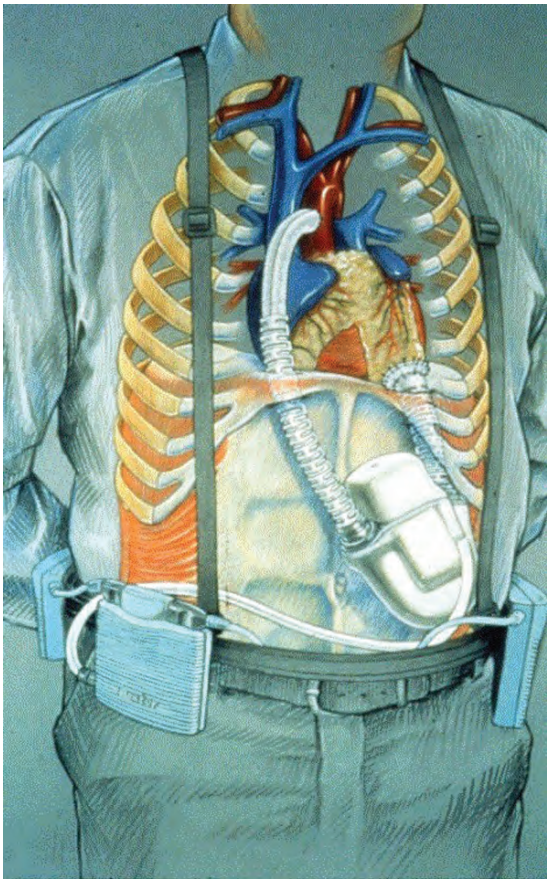


FIGURE 4.10. Diagram of the pulsatile Novacor LVAD which completely replaces the failing left ventricle.

Until recently, transplantation was mandatory for all patients in the United States committed to LVAD. However, when the native heart was excised during transplantation, it became clear to Frazier and others that some ventricles with idiopathic dilated cardiomyopathy had reverted toward normal size and weight.[58,59] Comparison of myocardial biopsies taken first at LVAD implantation, then during transplantation, showed regression of myocyte hypertrophy with decreased myocytolysis, myocardial fibrosis, and apoptosis (Figure 4.11). Myocyte genetic expression and cellular metabolism reverted toward normal.[60] Realization that recovering hearts were being discarded by transplantation led to the concept of mechanical bridge-to-myocardial recovery. Complementary to this approach is the development of much smaller and user-friendly axial flow and centrifugal blood pumps (Figure 4.12, a–f). In dilated cardiomyopathy patients, partial left ventricular unloading with a continuous flow device can provide a symbiotic relationship between the improving native heart and the blood pump (Figure 4.13). The majority of unloaded hearts show improvement in function and some LVADs can be removed with prolonged survival.[61]

The fact that LVAD use does not preclude transplantation but paradoxically improves posttransplant survival suggests that mechanical circulatory support could be used primarily for idiopathic dilated cardiomyopathy patents, leaving transplantation in reserve. After the REMATCH trial, blood pumps are already a widely accepted alternative to medical management in severely symptomatic non–transplant-eligible patients. With improved LVAD technology, the Health Care Advisory Board (USA) predicts 100,000 “lifetime” implants per year by 2010. There are early clues to the success of this approach. The first permanent Jarvik Flowmaker patient is NYHA I and leading a highly productive life, 4.5 years after his operation (Figure 4.14).

Some patients with idiopathic dilated cardiomyopathy, postpartum cardiomyopathy, and myocarditis have the potential to achieve bridge-to-myocardial recovery but there are many considerations before this promising approach can be translated into widespread clinical success. The first is a reliable LVAD for patients of all sizes. This should be

DropBooks

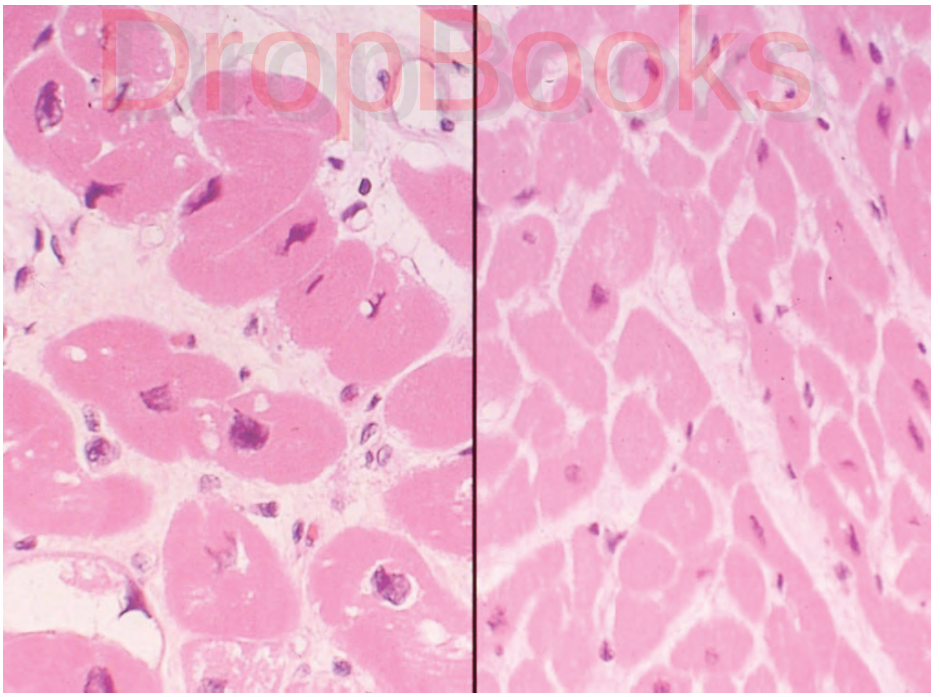
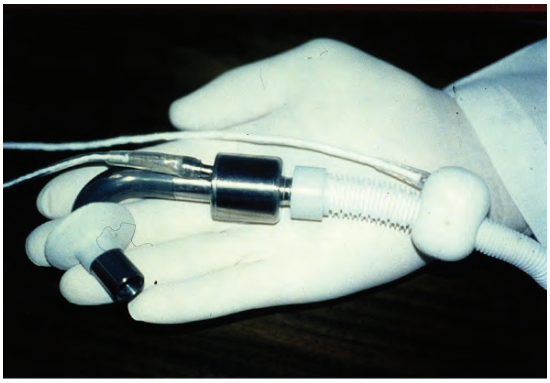


FIGURE 4.11. Histological samples of the left ventricular muscle taken at the time of LVAD implantation then after cardiac excision during transplantation. The hypertrophied myocytes have returned to normal size after chronic left ventricular unloading.



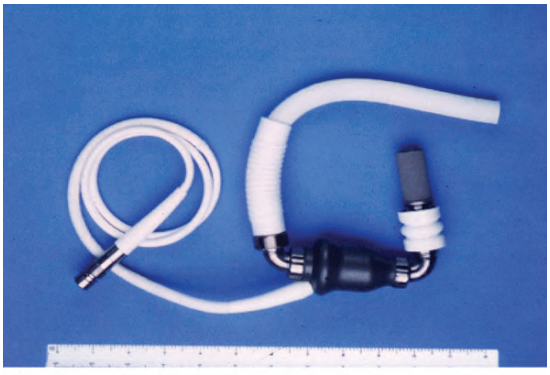
a



b



c



d



e

FIGURE 4.12. The new axial flow and centrifugal blood pumps. **a** Jarvik Flowmaker. **b** Micromed DeBakey VAD. **c** Berlin Incor. **d** Thermo Cardiosystem II. **e** Terumo left ventricular assist system (LVAS).

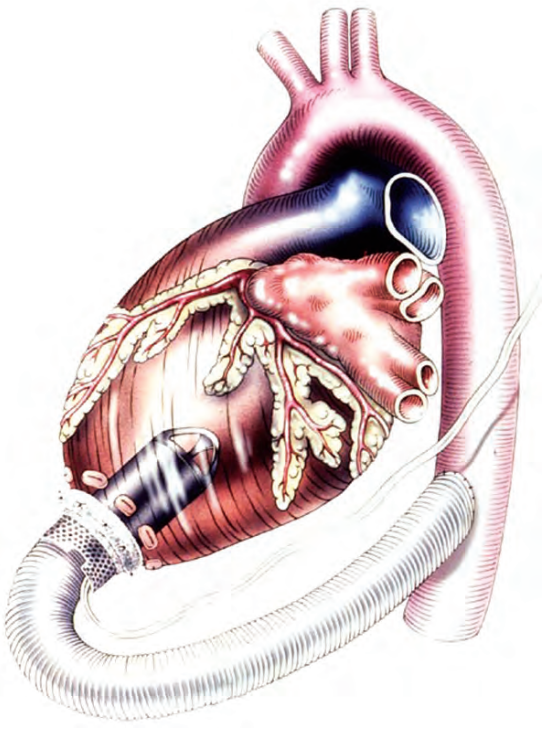


FIGURE 4.13. A Jarvik Flowmaker in situ. Pump flow is set to partially offload the left ventricle, thereby allowing antegrade ejection through the left ventricular outflow tract.



FIGURE 4.14. The first Jarvik Flowmaker "lifetime" implant patient 4.5 years after the operation. He leads a very productive life including long haul air travel.

DropBooks

relatively simple to implant and remove, and easy for the patient to control. The axial flow pumps are promising in this respect. Second, the LVAD must be implanted before myocardial fibrosis renders reversal of ventricular remodeling unachievable. Strategies to promote and sustain myocardial recovery with drugs, growth factors, gene therapy, and inhibitors of apoptosis are under investigation and markers for long-term recovery explored. In this respect, the Berlin group has used the disappearance from the serum of the autoantibody against the β-adrenergic receptor. They speculate that this reflects abatement of the immune process, which causes functional impairment.[62]

Clinical success with bridge-to-recovery highlights the importance of myocardial pathology. Patients with acute myocarditis or postpartum cardiomyopathy who are in terminal decline can be supported with an LVAD or BiVAD until resolution of the inflammatory process. Even those who require external cardiac massage and urgent cardiopulmonary bypass to sustain life before LVAD implantation



FIGURE 4.15. Infant with acute myocarditis and cardiac arrest who was bridge to recovery with the Berlin Heart.

can be restored to near-normal cardiac function[63] (Figure 4.15). For these categories of patients, a trial of circulatory support is arguably preferable to emergency transplantation and does not preclude this option in the event of failure to wean. In their study of weaning from chronic left ventricular support, the Berlin group compared factors which distinguished those with well-sustained recovery from others who slipped back into heart failure. Patients with long-

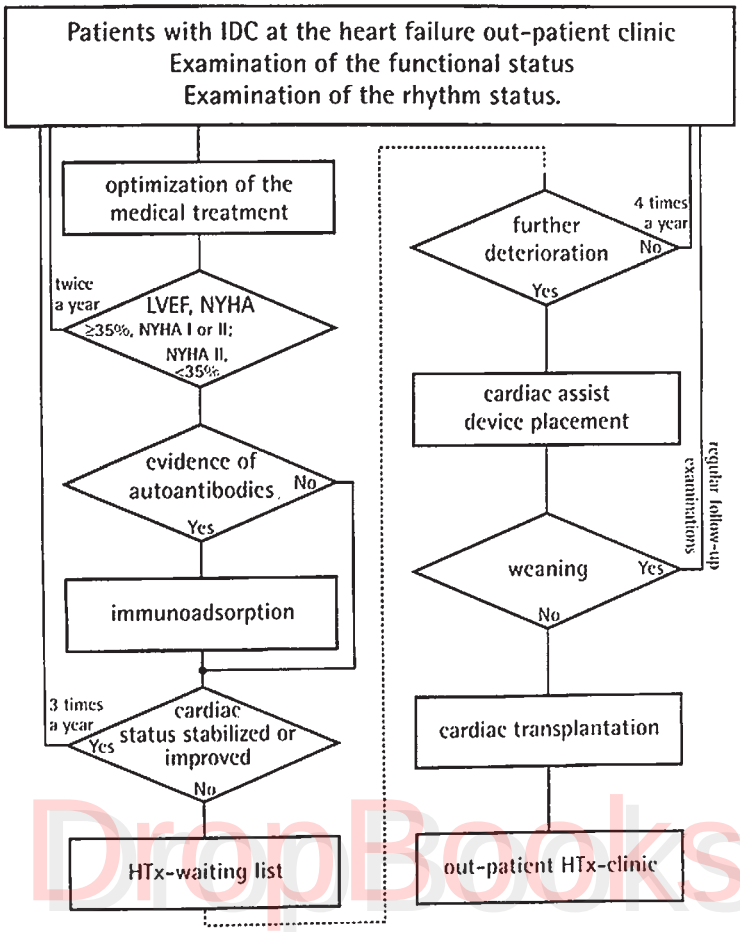
lasting recovery were younger, had a shorter history of heart failure, a more rapid improvement in cardiac performance, and needed a shorter duration of LVAD support before indices of cardiac volume and function justified device removal. The duration over which the autoantibody against the β-adrenergic receptors disappeared from the serum was shorter (8.8 weeks vs 9.7 weeks) in patients with sustainable recovery. Not different were mean age (41.5 years vs 50.3 years), mean LV end-diastolic diameter (LVEDD) at the time of device placement (75.2 mm vs 78.7 mm), LVEF (14.8% vs 17.0%), and mean LVEDD 2 months after LVAD placement (53.7 mm vs 55.6 mm).

The Berlin group concluded that an LVAD unloading period of between 8 and 10 weeks was optimal in patients destined for sustainable recovery and that longer support could lead to myocyte atrophy. Others have reservations about this limited duration and report success after much longer periods. However, Madigan et al. studied explanted LVAD unloaded heart between 8 and 155 days and found structural reverse remodeling to be complete to ~40 days.[64] Both LV chamber size and myocyte size had stabilized during this period. Collagen content was significantly increased in hearts supported for more than 40 days and this was consistent with a decrease in matrix metalloproteinase activity in these patients. Sarcoplasmic endoreticular calcium ATPase (SERCA2a) expression increased to normal levels by ~20 days of LVAD support. This information is difficult to translate into clinical practice when trying to make a decision regarding device removal. Nevertheless, all patients with idiopathic dilated cardiomyopathy who undergo LVAD implantation as potential bridge-to-transplant should be regarded as potential candidates for weaning without any certainty of reaching this goal.

Many serum markers have been shown to be pathologically altered at the time of device implantation and are subsequently improved or normalized at the time of removal. These include TNFα, matrix metallo proteinases (MMPs) -2 and -9, metallothionine, β-receptor density and responsiveness, apoptosis, atrial natriuretic factor, NO synthase, IL-6, and annexin-1, -2, -4, and -6. However, none of these parameters are predictive in determining the reversibility of cardiac malfunction before LVAD implantation. Rather, they are markers of chronic overload, sympathetic nervous system hyperactivity, and most likely, secondary phenomena of the disease.

Currently, the Berlin group considers the reversal of the inflammatory state in end-stage dilated cardiomyopathy as a precursor for reverse remodeling. To achieve this, they have treated dilated cardiomyopathy patients with immunoadsorption to remove the inflammatory autoantibodies. The Berlin-treatment algorithm is shown in Figure 4.16 and begins with optimal medical management. If this fails to improve cardiac status, immuno-adsorption is employed when pathological levels of A-β1-autoantibodies are demonstrated. If cardiac function continues to deteriorate and if criteria for heart transplantation are met, the patient is placed on the waiting list. In the event of critical low cardiac output before a donor becomes available, then mechanical circulatory support is instituted with a hope of reversing the ongoing cardiac impairment (Figure 4.17). If improvement does not occur, the LVAD functions as a bridge to transplantation. Given the potential for improvement, the decision to insert an LVAD is made relatively early since the prospect of reversal of the remodeling process deteriorates with time. Meanwhile, aggressive medical and antioxidative treatment of heart failure is pursued to enhance the chances of reverse remodeling. The patient is then followed by regular echocardiographic studies with the pump temporarily switched off to document LVEF and LVEDD. Before considering device explantation, these must reach at least 50% and 55 mm, respectively.

Hetzer and colleagues have reported successful explantation of 33 LVADs in dilated cardiomyopathy or myocarditis patients since 1995.[62] The mean duration since device removal for all 33 patients has been 6.5 years (range 1.3–9.3 years), 5-year survival after LVAD removal was 82%. Sustained improvement for more than 2 years after weaning occurred in 61% of the patients. The remainder relapsed into heart failure resulting in cardiac transplantation or death. Alhough markers of myocardial fibrosis were greatly elevated before LVAD implantation, the levels were not different between successfully weaned and relapsing patients. Irrespective of this, myocardial fibrosis seems to play an important role in the potential for improvement. By the time of LVAD implantation, many end-stage patients had myocardial ultrastructure which precludes reverse remodeling.



DropBooks

FIGURE 4.16. Berlin-treatment algorithm for patients with idiopathic dilated cardiomyopathy and worsening heart failure.

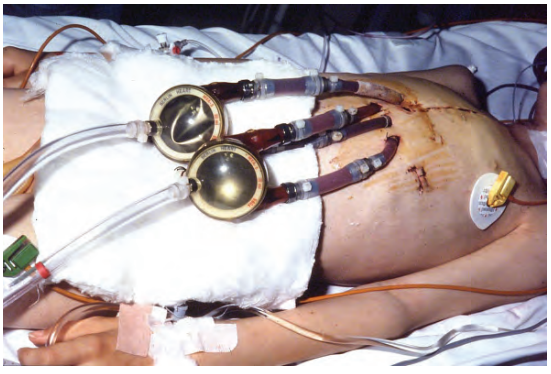


FIGURE 4.17. Child with idiopathic dilated cardiomyopathy with the Berlin Excor device awaiting transplantation.

4.8.5. Can the Chances of Recovery Be Improved?

Can the repair mechanism be enhanced to provide predictable and sustained recovery? Should earlier left ventricular unloading be employed with a newer device in order to improve the prospects for recovery? To what degree can adjunctive pharmacological or stem cell treatment be used to achieve this goal?

Yacoub et al. have suggested the use of the anabolic β2-agonist Clenbuterol to induce a so-called physiologic hypertrophy during unloading.[65] In rats the chronic administration of Clenbuterol (2 mg/kg/day vs placebo) produced significant hypertrophy and increased SERCA2a content with a prolonged action potential and increased oxidative carbohy-

drate utilization. The Harefield group combined LVAD unloading followed by Clenbuterol administration to produce cardiac hypertrophy. In an uncontrolled study the authors claim an increased likelihood of sustainable myocardial recovery after LVAD removal. However, other studies have found Clenbuterol to have myotoxic effects, which negatively influence cardiac function. Burniston et al. found subendocardial and skeletal muscle necrosis and apoptosis in rats given 5 mg Clenbuterol/kg.[66] Sleeper et al. administered clenbuterol (2.4 µg/kg) over 1 week to 20 horses.[67] This resulted in a significant decrease in myocardial function and increased aortic root dimensions, suggesting the risk of aneurysm formation. Further evidence is required before this β2-agonist is adopted in clinical practice. A larger multicentric trial is therefore planned.

4.9. Lifetime Circulatory Support as the Primary Treatment Option for Advanced Heart Failure

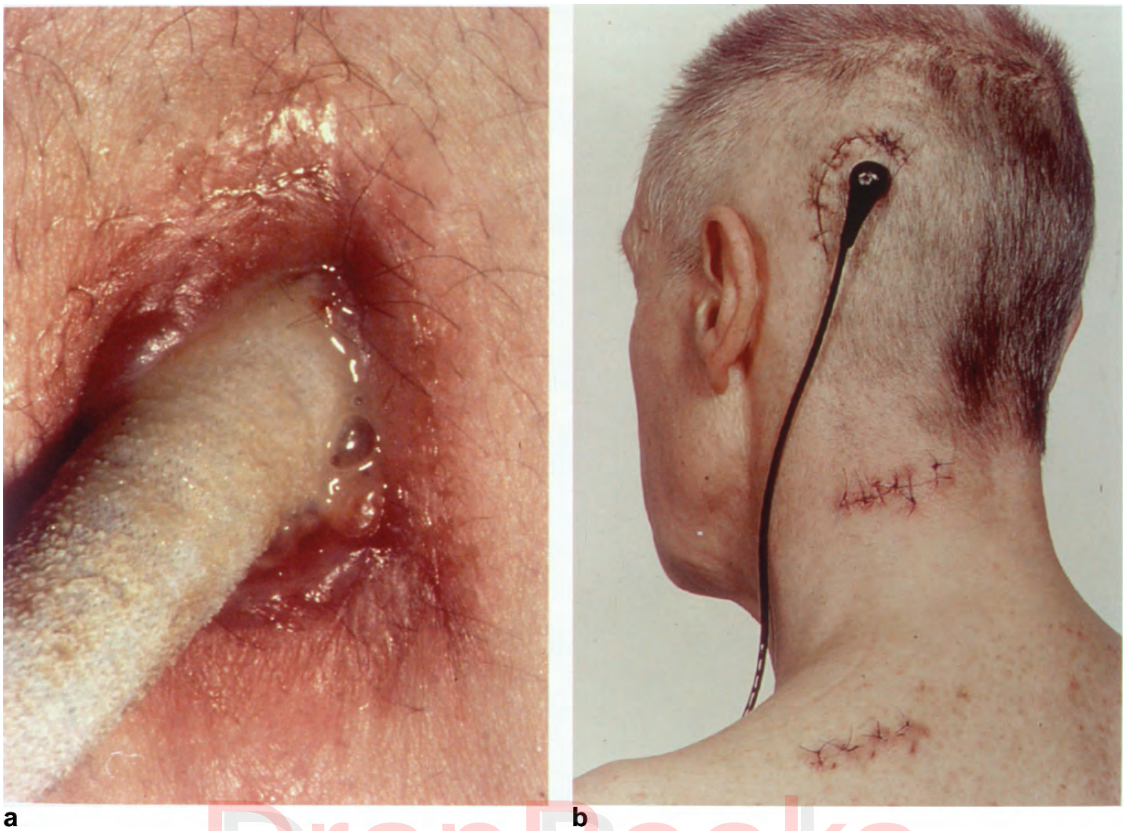
Three major developments have set the scene for indefinite mechanical circulatory support (lifetime or destination therapy) to develop into a primary treatment option for end-stage heart failure. First, a considerable amount of knowledge and expertise has been gained from long-term bridging to transplantation. This experience with pulsatile LVADs has provided up to 4 year survival with fewer device-related complications. LVAD blood flow reverses the heart failure syndrome, while mechanical unloading improves native cardiac function.[68] Second, the REMATCH trial has demonstrated improved survival with LVAD use over medical management in advanced heart failure.[26] REMATCH provides the evidence base for widespread LVAD use as an alternative treatment for non–transplant-eligible patients. Given that many transplant candidates die without receiving a donor organ, and that pre-transplant LVAD support has been shown to improve transplant survival, the question arises as to whether more transplant-eligible patients should be offered circulatory support as a therapeutic option. Third, the new axial flow and centrifugal pumps, which provide continuous flow, appear to be as effective as LVADs, which provide stroke volume and pulse pressure. These miniaturized blood pumps are silent, less obtrusive, and more user-friendly allowing early discharge from hospital and an active life in the community.[69] Avoidance of a transcutaneous abdominal driveline has reduced the risk of device infection[70] (Figure 4.18).

As an off-the-shelf commodity, LVADs are destined to join the pacemaker, cardiac resynchronization therapy, and the implantable defibrillator as first-line treatment of the failing heart. There are two major limitations to this progress. The first is cost of blood pumps, which must fall as their application becomes more widespread. The second is LVAD team expertise, which is currently limited to a small number of transplant centers.

4.9.1. Patient Selection for Lifetime Circulatory Support

Analysis of mortality in LVAD patients shows that many die as results of irreversible organ dysfunction or comorbidities present at the time of implantation.[26] These cases have been left too late. Until recently, patients considered for lifetime LVAD use have, by protocol, been ineligible for cardiac transplantation and in an advanced state of decompensation. Many already have multisite pacing, an implantable defibrillator, or are confined to hospital with intravenous inotropes or a balloon pump. The REMATCH study showed that when a patient is considered unsuitable for transplantation, by the same argument the patient may already have an unreasonably high risk for any type of cardiac surgery.[26] The decision to proceed to lifetime circulatory support should therefore be made on an elective basis and not as a salvage procedure. The patient should be a reasonable surgical candidate at acceptable risk. With safer, more user-friendly devices and less invasive operations, LVAD deployment should be brought forward out of the end-stage arena. With the expansion of information technology and increased patient awareness many heart failure patients now request LVAD therapy. Some LVAD patients will inevitably require transplantation due to progressive right heart failure. Paradoxically, other individuals who have been excluded from transplantation through renal impairment or increased pulmonary vascular resistance will improve sufficiently to achieve transplant status.

Identifying appropriate patients before the onset of irreversible organ dysfunction improves survival and reduces the degree of postoperative morbidity. In the presence of significant organ dysfunction,



DropBooks

FIGURE 4.18. **a** "First generation" LVAD driveline infection. **b** Skull-mounted power delivery based on cochlear implant technology. This system provides freedom from infection through rigid fixation in fat free highly vascular scalp skin.

the option of LVAD therapy is followed if the potential for organ recovery exists. The inclusion criteria for the REMATCH trial provide adequate guidelines for LVAD use. These patients were in chronic advanced heart failure (NYHA class IV) for at least 90 days though selection criteria were later broadened to NYHA class III or IV for 28 days but with recent requirement for intra-aortic balloon pump or inotrope support. The patient should have LVEF < 25% and peak exercise oxygen consumption < 12 mg/kg/min. While the great majority of REMATCH patient were inotrope or balloon pump dependent, it is widely recognized that lifetime LVAD implant should be performed electively before this premorbid state. Bridge-to-transplant selection criteria such as cardiac index ≤ 2 l/min/m^2, systolic blood pressure ≤ 80 mmHg, and pulmonary capillary wedge pressure ≥ 20 mmHg should not be a requirement for lifetime implant.

Perhaps the best patients for long-term LVAD therapy are those with idiopathic dilated cardiomyopathy, NYHA class III or IV with multiple hospital admission for medical stabilization, and an unacceptable quality of life at home. The use of prognostic models such as the Heart Failure Survival Score, which relies on the use of noninvasive clinical variables, may prove useful in identifying a homogeneous group of high-risk patients in this category.

4.9.2. Contraindications to LVAD Use

In many respects it easier to define contraindications to LVAD therapy. LVAD candidates should have no major irreversible cognitive defects that would limit their understanding of LVAD maintenance or ability to troubleshoot LVAD alarms. Stroke with motor impairment alone should not necessarily be a contraindication if sufficient family support is available. Patients with significant chronic obstructive or restrictive lung disease are at increased risk of mortality, particularly in the presence of pulmonary vascular disease and pulmonary hypertension that is

not reversed by vasodilator therapy. LVAD therapy reduces right ventricular afterload by reducing left ventricular filling pressure. In situations where pulmonary vascular resistance is fixed, unloading of the left ventricle may not achieve a significant reduction in right ventricular afterload. Restrictive pulmonary blood flow may impair LVAD filling in the presence of right-sided circulatory failure. Prolonged LVAD therapy will lower pulmonary vascular resistance and candidates are acceptable with resistance up to 6 Wood units or more in selected cases. The possibility of pulmonary thromboembolic disease should be considered and eliminated. There are no absolute criteria for pulmonary function testing since these may yield unreliable results in patients with pulmonary edema or cardiogenic shock. Generally, when pulmonary function testing is feasible, a forced expiratory volume at 1s of 50% of predicted, forced vital capacity of 50% of predicted, and diffusion capacity of the lung for carbon monoxide of 50% of predicted are adequate guidelines for accepting patients for LVAD therapy.

Although renal insufficiency is a significant risk factor for adverse LVAD outcome, careful evaluation must be performed in order not to exclude patients with the potential for recovery. The effects of low cardiac output must be differentiated from those of diabetic nephropathy or hypertensive renal disease. In contrast, significant hepatic dysfunction (assessed by total serum bilirubin, international normalized ratio (INR), or both) is an important marker for adverse outcome.[71] An INR exceeding 1.5, raised liver enzymes or bilirubin of >5 times normal, and established cirrhosis or hepatic fibrosis with portal hypertension are all definite contraindications to LVAD therapy. Even mild elevation of serum bilirubin and liver enzymes suggests the need for biventricular, as opposed to left ventricular, support.

Significant right heart failure is an important obstacle to providing lifetime circulatory support with an LVAD alone. Risk factors for postoperative right-sided circulatory failure include elevated central venous pressure (>16 mmHg), significant tricuspid insufficiency, right ventricular dysfunction despite low pulmonary artery pressure, low right ventricular stroke work index, and myocardial infarction with significant right ventricular and septal wall involvement.[72] Patients with an increased need for right ventricular assist device (RVAD) support may be an inappropriate group to consider for destination therapy until better RVADs or total artificial hearts are available.

Significant valvular pathology can have important adverse effects in LVAD patients. Aortic stenosis in the absence of regurgitation is not a contraindication to an LVAD implant. Mild-to-moderate aortic regurgitation can have a catastrophic impact on LVAD hemodynamics. Reductions in left ventricular pressure increase the pressure gradient across the aortic valve and increase the degree of aortic leak. Mild-to-moderate aortic insufficiency may become severe with initiation of LVAD support because of the fall in end-diastolic pressure and increase in aortic root pressure. Patients with a mechanical prosthesis in the aortic position must have this replaced with a bioprosthetic valve to avoid thrombosis. Even so, a bioprosthesis in the aortic position is also prone to thrombosis or fusion during complete unloading of the left ventricle. Fusion of native aortic valve leaflets has been reported with the pusher-plate devices, which actively empty the ventricle and prevent ejection.[73]

Patients with significant preexisting mitral stenosis require valvuloplasty before implantation of an LVAD but mitral regurgitation usually does not have an impact on LVAD function. However, elevation in pulmonary arterial pressure may persist with severe mitral regurgitation and reverse remodeling of the left ventricle can be adversely affected. In situations where weaning from LVAD support might be considerated, correction of the mitral pathology is necessary.

Adequate right heart function is extremely important to maintain pulmonary blood flow early after LVAD implantation. Severe tricuspid regurgitation impairs the forward flow of blood through the lungs particularly when pulmonary vascular resistance is elevated. Severe tricuspid regurgitation also contributes to elevated central venous pressure, hepatic congestion, and renal dysfunction. Tricuspid regurgitation may be present preoperatively in the setting of volume overload and biventricular failure, but may also develop after LVAD insertion if right ventricular dilatation occurs from leftward shift of the interventricular septum. Accordingly, tricuspid valve repair may be required to improve right-sided circulatory function.

Intra-cardiac shunts, such as patent foramen ovale (PFO) or atrial septal defect (ASD), may cause important right-to-left shunting and systemic desaturation. These must be eliminated before LVAD implant. Atrial flutter or fibrillation reduce right ventricular filling but are reasonably well tolerated by LVAD patients. Even ventricular fibrilla-

tion may occur unnoticed in LVAD patients when pulmonary vascular resistance is low.

4.10. Summary

The scope of heart failure surgery has progressed substantially over the past 10 years but awareness remains limited in the medical community. Nontransplant operations play an important role as the donor pool diminishes. Xenotransplantation is unlikely to provide a long-term "off-the-shelf" solution but mechanical devices are improving progressively toward this goal.

Decision making remains difficult as the evidence base is far from complete. Joint medical and surgical clinics are beneficial in this context. Many patients are referred late in the disease process and become high-risk candidates for conventional surgery. Satisfactory results may then depend upon the liberal use of the intra-aortic balloon pump or temporary circulatory support systems. Because of this, all specialized heart failure centers should gain access and experience with this technology. New approaches such as the use of autologous bone marrow stem cells provide an exiting insight into the future. As the demand increases, so does the need for innovation.

DropBooks

Key Points to Remember

- Cardiac transplantation remains the gold standard for end-stage heart advanced heart failure. This modality is limited by the number of donors and is reserved for younter patients with no major co-morbidities.
- Alternative surgical therapies must be explored for most patients that present with heart failure.
- These options include CABG, Mitral Valve Repair, Left Ventricular Reconstruction, Ventricular Assist Devices, etc.
- Decisions about alternative therapies and their choice is best made by multi-disciplinary teams.
- While experience is being gained in multiple surgical therapies, the exact risk profile and potential benefits about these strategies are still being worked out.

References

1. Yancy CW, Kaiser P, DiMaio JM, et al. Improved outcomes in patients awaiting heart transplantation: Making the case that Status 2 patients should not undergo transplantation [abstract]. *J Heart Lung Transplant*. 2002;21:69.
2. Deng MC. Orthotopic heart transplantation: Highlights and limitations. *Surg Clin North Am*. 2004;84:243-255.
3. Adamson PB, Abraham WT, Love C, et al. The evolving challenge of chronic heart failure management. *JACC*. 2004;44(7):1354.
4. Dor V. Surgical remodeling of the left ventricle. *Surg Clin N Am*. 2004;84:27-43.
5. Yamaguchi A, Ino T, Adachi H et al. Left ventricular volume predicts postoperative course in patients with ischemic cardiomyopathy. *Ann Thorac Surg*. 1998;65:434-438.
6. National Institute for Clinical Excellence Guideline no. 5. The Management of Chronic Heart Failure in Priming and Secondary Care. London: National Institute for Clinical Excellence; 2003.
7. McMurray JJ, Stewart S. Epidemiology, etiology and prognosis of heart failure. *Heart*. 2000;83:596-602.
8. SEOSI Investigators. Survey of heart failure in Italian hospital cardiology unit. Results of the SEOSI study. *Eur Heart J*. 1997; 18(9):1457-1464.
9. Westaby S, Banning A, Saito S, et al. Circulatory support as long-term treatment for heart failure. Experience with an intraventricular continuous flow pump. *Circulation*. 2002;105:2588-2591.
10. Di Carli MF, Maddhai J, Rockhsar S, et al. Long term survival of patients with coronary artery disease and left-ventricular dysfunction: Implication for the role of myocardial viability assessment in management decision. *J Thorac Cardiovasc Surg*. 1998;11:997-1004.
11. Yoshida F, Gould KL. Quantitative relation of myocardial infarct size and myocardial viability by positron emission tomography to left ventricular ejection fraction and 3 year mortality with and without revascularization. *JACC*. 1993;22:984-997.
12. Edmond M, Mock MB, Davis KB, et al. Long term survival of medically treated patients in the Coronary Artery Surgery Study (CASS). *Circulation*. 1994;90:2645-2657.
13. Rinaldi CA, Masani ND, Linka AZ, et al. Effect of repetitive episodes of exercise induced myocardial ischemia on left ventricular function in patients with chronic stable angina: Evidence for cumulative stunning or ischemic preconditioning? *Heart*. 1999;81:404-411.
14. Gerber BLJL, Vanovershelde JL, Bol A, et al. Myocardial blood flow, glucose uptake and recruitment of inotropic reserve in chronic left ventricular ischemic dysfunction. Implications for the pathophysiology of chronic myocardial hibernation. *Circulation*. 1994;94:651-659.

15. Adams JN, Norton M, Trent R, et al. Hibernated myocardium after acute myocardial infarction treated with thrombolysis. *Heart*. 1996;75:422-426.
16. Lee KS, Marvick TH, Cook SA, et al. Prognosis of patients with left ventricular dysfunction, with and without viable myocardium after myocardial infarction. Relative efficacy of medical therapy and revascularization. *Circulation*. 1994;90:2687-2694.
17. Westaby S. Coronary revascularization in ischemic cardiomyopathy. *Surg Clin North Am*. 2004;84:179-199.
18. Vanovershelde JL, Berger BL, D'Handt AM, et al. Preoperative selection of patients with severely impaired left ventricular function for coronary revascularization. Role of low dose dobutamine echocardiography and exercise redistribution-reinjection Thallium SPECT. *Circulation* 1995;92(suppl II):37-44.
19. Raymond JK, Edwin W, Allen R, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. *N Engl J Med*. 2000;343:1445-1453.
20. Mickleborough LL, Maruyama H, Yasushi T, et al. Results of revascularization in patients with severe left-ventricular dysfunction. *Circulation*. 1995;92(suppl II):73-79.
21. Bogaert J, Maes A, Van de Werf F, et al. Functional recovery of subepicardial myocardial tissue in transmural myocardial infarction after successful reperfusion. *Circulation*. 1999;99:36-43.
22. Cooley DA. Ventricula endoaneurysmorrhaphy: A simplified repair for extensive post-infarction aneurysm. *J Card Surg*. 1989;4:200-205.
23. Jatene AD. Left ventricular aneurysmectomy resection or reconstruction. *J Thorac Cardiovasc Surg*. 1985;89:321-331.
24. Dor V, Kreitmann P, Jourdan J, et al. Interest of "Physiological closure" (circumferential plasty on contractile areas) of left ventricle resection and endocardectomy for aneurysm of akinetic zone. Comparison with classical technique about a series of 209 left ventricular resections [abstract]. *J Cardiovasc Surg*. 1985;26:73.
25. Maisano F, Torracca L, Alfieri O, et al. The edge-to-edge technique: A simplified method to correct mitral insufficiency. *Eur J Cardiothorac Surg*. 1998;13:240-245.
26. Rose EA, Gelijns AL, Moskowitz AJ et al. Long-term use of left ventricular assist device for end-stage heart failure. *N Engl J Med*. 2001;345:435-443.
27. Hausmann H, Topp H, Siniawski H, et al. Decision making in the end stage coronary artery disease. Revascularization or heart transplantation. *Ann Thorac Surg*. 1997;64:1296-1302.
28. Tjan TDT, Kondruweit M, Scheld HH, et al. The bad ventricle—Revascularization versus transplantation. *J Thorac Cardiovasc Surg*. 2000;48:9-14.
29. Arnese M, Cornel JH, Salustri A, et al. Prediction of improvement of regional left ventricular function after surgical revascularization. A comparison of low-dose dobutamine echocardiography with 201TI single-photon emission computed tomography. *Circulation*. 1995;91:2748-2752.
30. Hass F, Jennen L, Heinzmann U, et al. Ischemically compromised myocardium different time course of functional recovery: Correlation with morphological alterations. *Eur J Cardiothorac Surg*. 2001;20:290-298.
31. Pagley PR, Beller GA, Watson DD, et al. Improved outcome after coronary artery bypass surgery in patients with ischemic cardiomyopathy and residual myocardial viability. *Circulation*. 1997;95:793-800.
32. Luciani GB, Faggani G, Razzaloni R, et al. Severe ischemic left ventricular failure: Coronary operation or heart transplantation? *Ann Thorac Surg*. 1993;55:719-723.
33. Bax JJ, Visser FC, Poldermans D, et al. Time course of functional recovery of stunned and hibernating segments after surgical revascularization. *Circulation*. 2001;104(suppl I):I.31314-I.31318.
34. Hass F, Jennen L, Heinzmann U, et al. Ischemically compromised myocardium different time course of functional recovery: Correlation with morphological alterations. *Eur J Cardiothorac Surg*. 2001;20:290-298.
35. Kim RJ, Wu E, Rafael A, et al. The use of contrast-enhanced magnetic resonance imaging to identify reversible myocardial dysfunction. *N Engl J Med*. 2000;343:1445-1453.
36. Maes A, Flameng W, Nuyts J et al. Histological alterations in chronically hypoperfused myocardium: Correlation with PET findings. *Circulation*. 1994;90:735-745.
37. Shan K, Bick RJ, Poindexter BJ, et al. Altered adrenergic receptor density in myocardial hibernation in humans. *Circulation*. 2000;102:2599-2606.
38. Dor V, Sabatier M, Di Donato M, et al. Efficacy of endoventricular patch plasty in large post infarction akinetic scar and severe left ventricular dysfunction: Comparison with a series of large dyskinetic scars. *J Thorac Cardiovasc Surg*. 1998;116:50-59.
39. Athanasulsas CL, Stanley AWH, Buckberg GD. Restoration of contractile function in the enlarged left ventricle by exclusion of remodeled akinetic anterior segment. *J Card Surg*. 1998;13:418-428.
40. Spotovitz HM, Spotnitz WD, Cotrell TS, et al. Cellular basis for volume related wall thickness changes in the rat left ventricle. *J Mol Cell Cardiol*. 1974;6:317-331.
41. Athanasuleas CL, Stanley AW Jr, Buckberg GD, et al. Surgical anterior ventricular endocardial restoration (SAVER) in the dilated remodeled ventricle after anterior myocardial infarction. RESTORE group. Reconstructive Endoventricular Surgery, returning Torsion Original Radius Elliptical Shape to the LV. *JACC*. 2001;37(5):1199-1209.

42. Stamm C, Kleine HD, Westphal B, et al. CABG and bone marrow stem cell transplantation after myocardial infarction. *Thorac Cardiovasc Surg*. 2004;52(3):152-158.
43. Perin EC, Dohmann HF, Borojevic R, et al. Transendocardial, autologous bone marrow cell transplantation for severe, chronic ischemic heart failure. *Circulation*. 2003;107(18):2294-2302.
44. Kirklin JK, McGiffin DC, Pinderski LJ, et al. Selection of patients and techniques of heart transplantation. *Surg Clin N Am*. 2004;84:257-287.
45. Deng MC. Orthotopic heart transplantation: Highlights and limitations. *Surg Clin North Am*. 2004;84:243-255.
46. Hosenpud JD, Bennett LE, Keck BM et al. Registry of the International Society for Heart and Lung Transplantation: 18th official report—2001. *J Heart Lung Transplant*. 2001;20:805-815.
47. Deng MC, De Meester JMJ, Smith JMA, et al. on behalf of COCPIT study group. The effect of receiving a heart transplant: Analysis of a national cohort entered onto waiting list, stratified by heart failure severity. *BMJ*. 2000;321:540-545.
48. Aaronson KD, Schwartz JS, Chen TMC, et al. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplantation evaluation. *Circulation*. 1997;95:2660-2667.
49. Shah NR, Rogers JD, Ewald GA et al. Survival of patients removed from the heart transplant waiting list. *J Thorac Cardiovasc Surg*. 2004;127:1481-1485.
50. Kirklin J, Miller L, Brown R, et al. Who is the most likely to enjoy long-term survival after cardiac transplantation with stratification in 10-year multi-institutional experience [abstract]. *J Hear Lung Transplant*. 2001;20:168.
51. Morgan JA, John R, Lee BJ, et al. Is severe right ventricular failure in left ventricular assist device recipients a risk factor for unsuccessful bridging to transplant and post-transplant mortality. *Ann Thorac Surg*. 2004 Mar;77(3):859-863.
52. Copeland JG, Smith RG, Arabia FA, et al. CardioWest Total Artificial Heart Investigators. Cardiac replacement with a total artificial heart as a bridge to transplantation. *N Engl J Med*. 2004 Aug 26;351(9):859-867.
53. Bolling SF, Pagani FD, Deeb GM, et al. Intermediate term outcome of mitral reconstruction in cardiomyopathy. *J Thorac Cardiovasc Surg*. 1998;115:381-388.
54. Konertz WF, Kleber FX, Dushe S, et al. Efficacy trends with the Acorn cardiac support device in patients with advanced heart failure. *J Heart Fail*. 2001;7:39.
55. Sabbah HN, Chaudhory PA, Paone G, et al. Passive ventricular constraint with the Acorn prosthetic jacket prevents progressive left ventricular dilatation and improve ejection fraction in dogs with moderate heart failure [abstract]. *JACC*. 1999;33(suppl A):A207.
56. Batista RJV, Verde J, Nery P, et al. Partial left ventriculectomy to treat end-stage heart disease. *Ann Thorac Surg*. 1997;64:634-638.
57. Suma H, Isomura T, Horii T et al. Two-year experience of the Batista operation for nonischemic cardiomyopathy. *J Cardiol*. 1999;32:269-276.
58. Frazier OH, Benedict CR, Radovancevic B, et al. Improved left ventricular function after chronic left ventricular unloading. *Ann Thorac Surg*. 1996;62(3):675-682.
59. Loebe M, Muller J, Hetzer R. Ventricular assistance for recovery of cardiac failure. *Curr Opin Cardiol*. 1999;14(3):234-248.
60. Zhang J, Narula J. Molecular Biology of myocardial recovery. *Surg Clin N Am*. 2004;84:223-242.
61. Mueller J, Wallukat G, Weng Y, et al. Predictive factors for weaning from a cardiac assist device. An analysis of clinical, gene expression and protein data. *J heart Lung Transplant*. 2001;20(2):202.
62. Hetzer R, Muller J, Weng Y, et al. Cardiac recovery in dilated cardiomyopathy by unloading with a left ventricular assist device. *Ann Thorac Surg*. 1999;68:742-749.
63. Entwistle JWC III. Short- and long-term mechanical ventricular assistance towards myocardial recovery. *Surg Clin N Am*. 2004;84:201-221.
64. Madigan JD, Barbone A, Choudhri AF, et al. Time course of reverse remodeling of the left ventricle during support with a left ventricular assist device. *J Thorac Cardiovasc Surg*. 2001;121(5):902-908.
65. Hon JK, Yacoub MH. Bridge to recovery with the use of left ventricular assist device and clenbuterol. *Ann Thorac Surg* 2003;75:S36-S41.
66. Burniston JG, Ng Y, Clark WA, et al. Myotoxic effects of clenbuterol in the rat heart and soleus muscle. *J Appl Physiol*. 2002;93:1824-1832.
67. Sleeper MM, Kearns CF, McKeever KH. Chronic clenbuterol administration negatively alters cardiac function. *Med Sci Sports Exerc*. 2002;34:643-650.
68. Frazier OH, Rose EA, McCarthy P, et al. Improved mortality and rehabilitation of transplant candidates treated with long-term implantable assist system. *Ann Thorac Surg*. 1995;222:327-336.
69. Westaby S. Ventricular assist device as destination therapy. *Surg Clin N Am*. 2004;84:91-123.
70. McCarthy PM, Schmitt SK, Vargo RL, et al. Implantable LVAD infections: Implications for permanent use of the device. *Ann Thorac Surg*. 1996;61:359-365.
71. Masai T, Sawa Y, Ohtake S, et al. Hepatic dysfunction after left ventricular mechanical assist in patients with end-stage heart failure: Role of inflammatory response and hepatic microcirculation. *Ann Thorac Surg*. 2002;73:549-555.
72. Ochiai Y, McCarthy PM, Smedira NG, et al. Predictors of severe right ventricular failure after implantable left ventricular assist device insertion: Analysis of 245 patients. *Circulation*. 2002;106(12 Suppl 1):I198-I202.
73. Rose AG, Park SJ, Bank AJ, et al. Partial aortic valve fusion induced by left ventricular assist device. *Ann Thorac Surg*. 2000 Oct;70(4):1270-1274.

DropBooks

5
Transplantation for End-Stage Heart Disease

David C. McGiffin and James K. Kirklin

The history of cardiac transplantation is an intriguing story which started as a clinical experiment 30 years ago resulting in depressingly poor results to the point that the procedure risked abandonment as futile therapy. An era of renaissance emerged coincident with the introduction of cyclosporine-based immunosuppression evolving into an era where cardiac transplantation was regarded as the primary and "gold standard" therapy for end-stage heart disease. No doubt other factors and experience played into this development. Cardiac transplantation now, however, has entered quite a different era as a result of the considerable imbalance between the number of available donor hearts and the much greater number of potential recipients as well as the imperfections in current immunosuppression and the life-limiting effects of chronic rejection manifesting as coronary allograft vasculopathy. In this present era, cardiac transplantation is but one of many surgical and nonsurgical alternatives for patients with end-stage heart disease. The challenge in this era is the accurate assignment of one or more therapies for an individual patient to produce the maximal benefit in terms of life expectancy and quality of life. The appropriate assignment of therapy for an individual patient is predicated upon the generation of patient-specific (which implies risk adjusted) time-related survival estimates for these various therapies, but currently the widespread application of this process remains elusive.

Although the concept of *survival benefit margin*[1] may not necessarily be articulated, it is embodied in the decision-making processes throughout transplantation for an individual patient. It permeates decision making regarding alternative surgical and nonsurgical therapies, listing for transplantation, donor selection, and donor-recipient matching. In essence, the concept of survival benefit margin refers to the difference in predicted survival for an individual patient between the natural history without transplantation and that of cardiac transplantation. Ultimately, decision making for an individual patient represents a very difficult balance between maximizing survival benefit margin (such as recipient B in Figure 5.1), but with the potential for inferior survival compared with a recipient whose survival benefit margin is not as great (recipient A in Figure 5.1), even though long-term survival is superior. It is the improving results of cardiac transplantation, the results of surgical and nonsurgical alternatives to transplantation, and the changing landscape of donor organ availability (such as the use of "marginal" donor hearts) that makes application of these important allocation principles so challenging.

5.1. Recipient Evaluation, Selection, and Listing for Transplantation

The evaluation process for patients with end-stage heart disease integrates the goals of avoiding cardiac transplantation either prematurely or too late in the natural history of the disease, considering alternative therapies to cardiac transplantation, and detecting comorbidity that would contraindicate transplantation. Therefore, the approach to patients

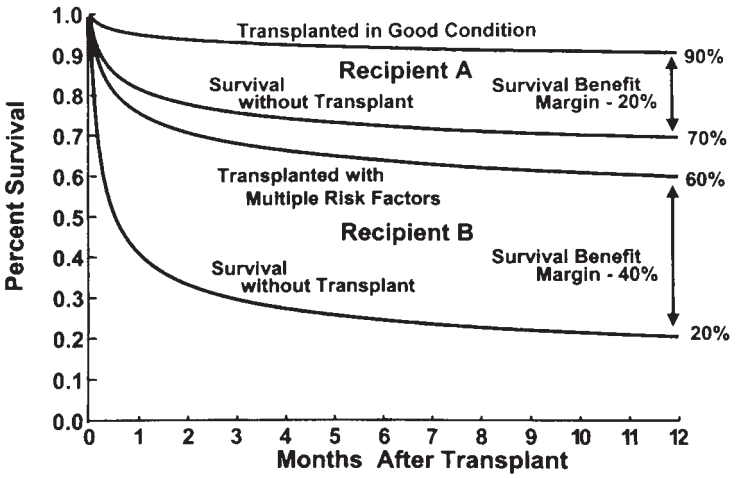


FIGURE 5.1. Hypothetical depiction of survival benefit margin for a stable recipient in good condition (Recipient A) and a seriously ill recipient with multiple risk factors (Recipient B). (Kirklin et al.,[1] with permission).

with end-stage heart disease[1] is to (a) detect potentially reversible causes of heart failure, (b) evaluate severity of heart failure and functional capacity, (c) tailor medical therapy to relieve symptoms, (d) assess risks of rapid progression of heart failure or sudden death, (e) identify indications for transplantation, (f) exclude contraindications to transplantation, (g) and throughout the evaluation and listing process, continue to manage heart failure and regularly reevaluate the patient to ensure appropriateness of the therapeutic strategy.

Implicit in the timing for listing for cardiac transplantation is the assumption that the natural history of end-stage heart disease can be predicted, but unfortunately this information is still quite imperfect. There have been a number of attempts made to develop predictive equations for survival with advanced heart failure, and this information is important to incorporate into the decision-making process; for example, the Heart Failure Survival Score (HFSS) from Columbia-Presbyterian Medical Center.[2,3] This score was developed using multivariable methods to determine both noninvasive and invasively derived variables that predict either death without transplantation or the need for urgent cardiac transplantation. A final noninvasive predictive model was developed containing the following variables: ischemic cardiomyopathy, resting heart rate, left ventricular ejection fraction, intraventricular conduction delay (QRS duration ≥ 0.12 s), mean resting blood pressure, peak $\dot{V}O_2$, and serum sodium. The addition of invasive variables, such as right heart catheterization information, did not increase the discrimination of the model. From this model a heart failure survival score was developed and patients could be stratified into groups with quite different survival (Figure 5.2). On the basis of this stratification, patients in the medium and high-risk strata would likely have better survival with cardiac transplantation. This type of modeling may allow more rational decision making in the management of patients with end-stage heart disease.

A protocol for potential recipient evaluation is outlined in Table 5.1. Part of the evaluation includes determination of the immunologic status for the purpose of recipient–donor matching and assessment of the adequacy of the patient's social support and financial resources since deficiencies in these areas may be just as threatening to survival and quality of life as any comorbid medical condition.

General guidelines have been established as *indications* for cardiac transplantation[1] (Table 5.2) although increasing knowledge of the results of alternative therapies for patients with heart failure, improving results of cardiac transplantation with the seemingly immutable shortage of donor hearts, and the specific criteria that precipitates listing for transplantation are still very much in flux. However,

DropBooks

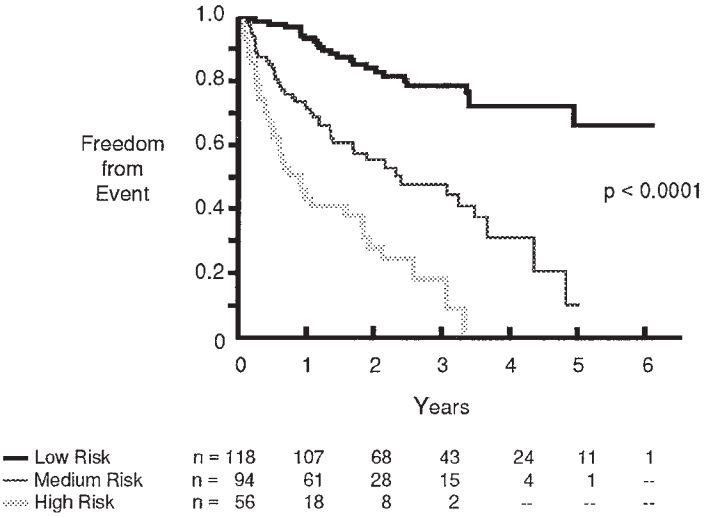


FIGURE 5.2. Event-free survival of patients with advanced heart failure, stratified into low-, medium-, and high-prognostic-score risk groups on the basis of a multivariable model incorporating noninvasively-derived risk factors. The number of patients remaining available for follow-up for each risk group is shown below each graph. An event is defined as death without transplantation or UNOS status I transplant (Aaronson et al.,[3] with permission).

TABLE 5.1. Evaluation protocol for cardiac transplantation.

General
Complete history and physical examination
Nutritional status evaluation[a]
Blood chemistries including liver and renal profiles [bilirubin, SGOT (AST), alkaline phosphatase, BUN, creatinine, calcium, phosphorus, magnesium]
Hematology and coagulation profile [complete blood cell count, differential, platelet count, prothrombin time (or International Normalized Ratio), partial thromboplastin time, fibrinogen]
Serum electrolytes
Lipid profile[a]
Urinalysis
24-h urine for creatinine clearance (and protein if diabetic or urinalysis positive for protein[a]
Nuclear renal scan with measurement of effective renal plasma flow[a] (ERPF)
Pulmonary function testing with arterial blood gases
Ventilation-perfusion scan[a]
Stool for heme
Mammography[a]
Prostate-specific antibody (PSA)[a]
Abdominal ultrasound study (liver, pancreas, gall bladder, and kidney evaluation)
Carotid ultrasound
Social evaluation
Psychiatric evaluation
Neuropsychiatric evaluation (neurocognitive evaluation)[a]
Dental evaluation
Sinus films[a]
Cardiovascular
Electrocardiogram
Chest radiograph (PA and lateral)
Two-dimensional echocardiogram with Doppler study
Exercise test with oxygen consumption (peak Vo_2)
Right-heart catheterization with detailed hemodynamic evaluation
Shunt series[a]

(continued)

TABLE 5.1. (continued)

Left-heart catheterization with coronary angiography[a]
Myocardial biopsy[a]
Radionuclide angiogram (gated blood pool study)[a]
Nuclear imaging study for myocardial viability (thallium-201 or positron emission tomography)[a]
Holter monitor for arrhythmias (if ischemic cardiomyopathy)[a]
Immunology
ABO blood type and antibody screen
Panel-reactive antibody (PRA) screen
Human leukocyte antigen (HLA) typing (if to be listed for transplantation)
Infectious Disease Screening
Serologies for hepatitis A, B, and C; Herpes virus, human immunodeficieincy virus (HIV), cytomegalovirus (CMV), toxoplasmosis, varicella, rubella, Epstein-Barr virus, veneral disease research laboratory (VDRL), Lyme titers[a], histoplasmosis, and coccidioidomycosis complement-fixing antibodies[a]
Throat swab for viral cultures (CMV, adenovirus, Herpes simplex virus)[a]
Urine culture and sensitivity[a]
Stool for ova and parasites[a]
PPD (purified protein derivative) skin test with controls (i.e., mumps, dermatophytin, histoplasmosis, and coccidioidomycosis[a])

Kirklin et al.,[1] with permission.
[a]Only performed if appropriate or indicated.

TABLE 5.2. General indications for cardiac transplantation.

Criteria for consideration of heart transplantation in advanced heart failure
Significant functional limitation (NYHA class III–IV heart failure) despite maximum medical therapy that includes digitalis, diuretics, and vasodilators, preferably angiotensin-converting enzyme inhibitors, at maximum tolerated doses.
Refractory angina or refractory life-threatening arrhythmia
Exclusion of all surgical alternatives to transplantation, such as the following:
Revascularization for significant reversible ischemia
Valve replacement for severe aortic valve disease
Valve replacement or repair for severe mitral regurgitation
Appropriate ventricular remodeling procedures
Indications for cardiac transplantation determined by severity of heart failure despite optimal therapy
Definite indications
$\dot{V}O_2$ max < 10 ml/kg/min
NYHA Class IV
History of recurrent hospitalization for congestive heart failure
Refractory ischemia with inoperable coronary artery disease and left ventricular ejection fraction < 20%
Recurrent symptomatic ventricular arrhythmias
Probable indications
$\dot{V}O_2$ max < 14 mg/kg/min (or higher with multiple other risk factors)
NYHA class III–IV
Recent hospitalizations for congestive heart failure
Unstable angina not amenable to coronary artery bypass grafting, percutaneous transluminal coronary angioplasty with left ventricular ejection fraction < 0.25%

Kirklin et al. 2004, with permission[1]

DropBooks

it is generally accepted that patients should be considered for cardiac transplantation when they have New York Heart Association (NYHA) class III–IV heart failure, severe reduction in the quality of life due to their symptoms, and a predicted 2-year survival of less than approximately 60%.

Transplantation of United Network for Organ Sharing (UNOS) status II patients is a contentious issue since some studies have questioned the survival advantage for these patients with cardiac transplantation.[4,5] However, the issue is complicated by the apparent survival advantage in pediatric

Table 5.3. Contraindications to cardiac transplantation.

General Contraindications
Presence of any noncardiac condition that would itself shorten life expectancy or increase the risk of death from rejection or complications of immunosuppression
Specific Contraindications[a]
Age greater than about 65 years (program variability)
Active infection
Active ulcer disease
Severe diabetes mellitus with end-organ damage
Severe peripheral vascular or cerebrovascular disease
Coexisting neoplasm
Morbid obesity
Creatinine clearance < 40–50 ml/min, effective renal plasma flow (ERPF) < 200 ml/min[b]
Bilirubin > 2.5 mg/dl, transaminases > 2× normal[c]
Severe pulmonary dysfunction with FVC and FEV_1 < about 40% of predicted, especially with intrinsic lung disease
Pulmonary artery systolic pressure > 60 mmHg, mean transpulmonary gradient > 15mmHg or pulmonary vascular resistance > 5 Wood units[d]
Acute pulmonary thromboembolism
Active diverticulitis
High risk of life-threatening noncompliance
Inability to make strong commitment to transplantation
Cognitive impairment severe enough to limit comprehension of medical regimen
Psychiatric instability severe enough to jeopardize incentive for adherence to medical regimen
History of recent smoking (within 6 months)
History of recurring alcohol or drug abuse
Failure of established stable address or telephone number
Previous demonstration of repeated noncompliance with medication or follow-up
Lack of independent family or social support system
History of marked depression or emotional instability

Kirklin et al.,[1] with permission.

[a] May be relative or absolute, depending on severity or program philosophy.

[b] May be suitable for cardiac transplantation if inotropic support and hemodynamic management produce a creatinine < 2 mg% and creatinine clearance > 50 ml/min. Transplantation may also be advisable as combined heart–kidney transplant.

[c] Requires liver biopsy to exclude cirrhosis or other intrinsic liver disease.

[d] These apply only if the increased resistance is largely nonreactive (fixed).

heart transplantation (for status II recipients)[6] and the paucity of available information for prediction of the "natural history" within various subsets of status II adult patients.

There are a number of *contraindications* for cardiac transplantation[1] (Table 5.3). Although there would be general agreement that many of these contraindications are absolute, some would be regarded as relative, based on programmatic experiential reasons or risk/benefit considerations in an individual patient. For example, in many programs renal dysfunction (due to intrinsic renal disease or associated with heart failure) would not be regarded as a contraindication as excellent results can be achieved with combined heart–kidney transplantation.

The current etiologies of heart failure that are considered for transplantation are predominantly ischemic heart disease and dilated cardiomyopathy. A much smaller proportion of adult patients undergo transplantation for heart failure associated with previous correction of congenital heart disease such as a failing Fontan procedure, end-stage valvular heart disease, and retransplantation.

Cardiac retransplantation requires special comment. Current information[7] suggests that patients with early graft failure or graft failure due to acute rejection should not be offered retransplantation because of inferior survival compared to primary cardiac transplantation (Figure 5.3). However, retransplantation due to coronary allograft vasculopathy or other nonspecific graft failure is an appropriate indication for retransplantation since the survival of these patients is very similar to that of patients undergoing primary cardiac transplantation (Figure 5.4).

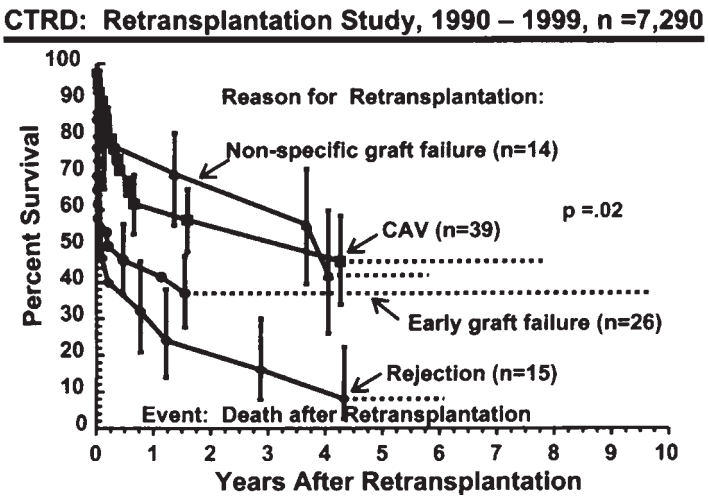


FIGURE 5.3. Actuarial survival (Kaplan-Meier) stratified by reason for cardiac retransplantation. Vertical bars represent the standard error. (Radovancevic et al.,[7] with permission).

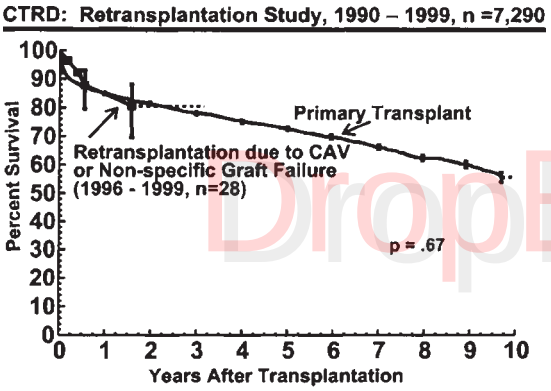


FIGURE 5.4. Actuarial survival (Kaplan-Meier) for patients undergoing cardiac retransplantation for CAV or nonspecific graft failure (era 1996–1999) compared with that of patients undergoing primary cardiac transplantation. Vertical bars represent the standard error. (Radovancevic et al.,[7] with permission).

In the United States, patients are *listed for cardiac transplantation* with UNOS. This organization is responsible for the donor organ distribution system. Table 5.4[8] is a simplification of the policy for allocation of thoracic organs, which in essence allocates donor hearts based on priority reflecting the severity of illness. Similar organ allocation or placement agencies exist in Australia, Europe, the United Kingdom, and other areas where cardiac transplantation is offered.

5.2. Cardiac Donor Evaluation

Cardiac transplantation is possible only through unselfish organ donation by families at the worst possible time of their lives. The procurement of hearts from heart-beating donors is predicated upon the worldwide acceptance of brain death criteria. The volume of cardiac transplantation is limited by donor heart availability and there will never be enough donor hearts available to fill the need. The immutable shortage persists despite intensive educational programs, and in some European countries "presumed consent" laws as well as in the United States "required request" protocols, that mandate that hospitals approach families of brain dead patients regarding organ donation.

5.2.1. Effects of Brain Death on Cardiac Function

Brain death is a hostile environment for the heart and impacts cardiac transplantation by causing donor heart dysfunction. This may preclude use of the donor heart or contribute to the not insignificant incidence of primary graft failure following cardiac transplantation. The causes of donor heart dysfunction can be conceptualized into two phases—those occurring with the Cushing response and those following dissipation of the Cushing response (Figure 5.5).

DropBooks

TABLE 5.4. Description of UNOS status levels.

Status IA	Must be an inpatient with at least one of the following: Life expectancy less than 7 days VAD-related thromboembolism VAD-related infection (including the pocket and the driveline) ECMO (extra-corporeal membrane oxygenator) Intra-aortic balloon pump with inotropic criteria Continuous invasive hemodynamic monitoring with inotropic criteria Life-threatening arrhythmias Mechanical ventilation 30 days following medical stabilization after VAD implantation
Status IB	Inotrope-dependent VAD not meeting criteria for IA status
Status II	Not inotrope-dependent and without a VAD
Status VII	Inactive on list either because of improved clinical status or short-term contraindications to cardiac transplantation (i.e., active infection)

Inotrope Criteria for Status IA
(1) Two or more inotropes regardless of dose
(2) IV milrinone at least 0.5 mcg/kg/min via continuous infusion
(3) IV dobutamine at least 7.5 mcg/kg/min via continuous infusion

Boyle,[8] with permission.
UNOS United Network for Organ Sharing, *VAD* ventricular assist device

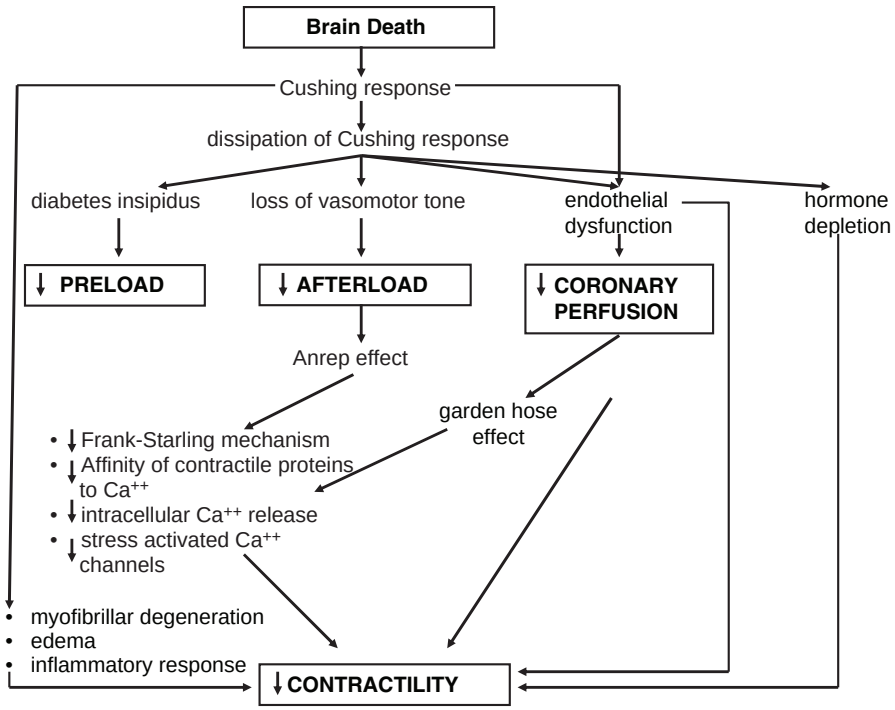


FIGURE 5.5. Pathophysiological effects of brain death on the cardiovascular system following brain death. (Based in part on Szabo).[11]

The Cushing response is a "catecholamine storm" inducing hypertension, tachycardia, intense vasoconstriction, and an increase in myocardial oxygen demand, resulting in myocardial ischemia. The injury to the myocardium is a phenomenon known as myofibrillar degeneration (which is also known as contraction band necrosis or coagulative myocytolysis) which is distinct from the coagulation necrosis seen in acute myocardial infarction. Myofibrillar degeneration is characterized histologically by the death of myofibers in a hypercontracted state with obvious contraction bands. The other important histological feature that may be seen is a mononuclear cellular infiltrate, which is evidence of the intense inflammatory response known to be activated with brain death. There are experimental studies[9,10] that have detected upregulation of cytokines, chemokines, adhesion molecules, and immunoregulatory molecules. This happens along with leukocyte activation. All of these likely have a role in endothelial cell injury and activation. When this period of intense sympathetic activity is dissipated, there is loss of sympathetic tone with a massive reduction in systemic vascular resistance contributing to the second phase of potential myocardial injury. This phase of injury can be conceptualized as abnormal loading conditions and coronary perfusion.[11] Intervention and donor management in this phase, offers some hope of retrieving donor hearts that would ordinarily have been lost. There is experimental evidence that if coronary perfusion pressure is decoupled from aortic pressure and returned to pre–brain death levels, coronary blood flow and myocardial contractility can also be restored.[12] The exact mechanisms of how the loading conditions and coronary perfusion down-regulate myocardial contractility are not completely clarified, but may occur through the Frank-Starling mechanism or other less well-characterized mechanisms such as the Anrep effect[13,14] (maintenance of optimal stroke work over a range of afterload conditions controlled through cellular mechanism) and the garden hose effect,[15,16] which has been described in isolated heart preparations. This effect refers to the relationship between increased coronary perfusion pressure and increased contractility by direct intramyocardial vessel stretch and this mechanism may possibly come into play at a level of coronary perfusion pressure below which autoregulation is no longer operational.

5.2.2. Screening for Cardiac Donation

Following declaration of brain death and obtaining consent, the process of determining suitability for cardiac donation is allowed to proceed. The screening process[17] (Table 5.5) has a number of goals. The general organ donation screening is to prevent the transmission of malignancies (although the presence of primary central nervous system tumors is acceptable) or the transmission of viral disease such as hepatitis B and C, HIV infection, or HTLV-1. The presence of donor bloodstream infection is a contraindication to cardiac donation although donors with localized infection (particularly the lung) will still be suitable. Exclusion of coronary artery disease (CAD) is necessary in cardiac donor males older than 40 years and females older than 45 years, although these age criteria may vary depending on the presence or absence of risk factors for CAD. The determined adequacy of cardiac function must usually be delayed until hemodynamic stability has been obtained. Many donors have deranged loading conditions due to the very low systemic vascular resistance together with a low preload associated with the aggressive

DropBooks

Table 5.5. Screening criteria for cardiac donation.

General organ donation screening
Absence of infection
Hepatitis B and C, HIV, and HTLV-1 serology
Negative blood cultures
Psychosocial/lifestyle screening
Absence of malignancy (excluding primary CNS tumors)
Screening for coronary disease
Age usually less than 55
Coronary angiography if possible:
Men > 40 years
Women > 45 years
No pathologic Q waves on ECG
No history of insulin-requiring diabetes
No other prior cardiac history
Screening for cardiac function
No requirement for high-dose inotropic support (after volume replacement)
No prolonged resuscitation
Normal echocardiogram (mild segmental wall motion or mitral prolapse not a contraindication, expanded criteria using moderate wall motion abnormalities if normal coronaries)

Hosenpud,[17] with permission.
CNS central nervous system.

diuresis often used to control cerebral edema prior to progression to brain death and/or diabetes insipidus following brain death. As a consequence, these donors are often on high-dose adrenergic support, which, with optimization of loading conditions, can be rapidly weaned. At that stage, the echocardiogram has become the most useful test to evaluate left and right ventricular systolic function.

5.2.3. The Effect of Donor Factors and Ischemic Time on Graft Function

Early graft failure represents an important cause of morbidity and mortality after cardiac transplantation, and is impacted by donor factors (such as donor age, inotropic requirements, echocardiographic abnormalities) and ischemic time. However, when making a decision regarding the suitability of a particular donor, these factors cannot be considered in isolation since they are all inextricably interrelated. A relationship exists between older donor age and the probability of graft failure and this risk is further exacerbated by increasing ischemic time[18] (Figure 5.6). This effect is no doubt related to the overall decline in myocardial reserves associated with increasing age. Similarly, the risk of early graft failure is increased by the presence of an echocardiographic wall motion abnormality, an effect which becomes increasingly pronounced with increasing donor age[19] (Figure 5.7).

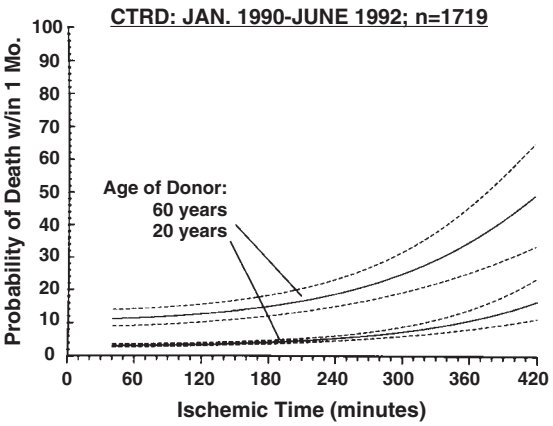


FIGURE 5.6. Nomogram from donor/recipient multivariable analysis in hazard function domain depicts varying ischemic time for two donors, aged 20 and 60 years. Equation is solved for 50-year-old male recipient who is not on ventilator, not on ventricular assist device, has undergone no previous sternotomies, and has pulmonary vascular resistance of 2.2 Wood Units and male donor who is not diabetic, not receiving inotropic support, did not die of cardiac arrest, and has no diffuse wall motion abnormalities. Dashed lines represent 70% confidence limits around parametric curves. (Young et al.,[18] with permission).

5.2.4. Special Situations

In order to increase the number of available donor hearts, a number of donor conditions may still be considered compatible with successful transplantation.

Donor *CAD* is not necessarily a contraindication to transplantation and coronary bypass surgery has been utilized on donor hearts. This concept of matching "recipients who would not ordinarily meet criteria for cardiac transplantation or retransplantation" to "marginal" donor hearts has given rise to the concept of the "alternate list."[20] Survival of recipients with donor hearts that have undergone coronary bypass surgery appears to be very acceptable.[21]

Some donor hearts with *valvular disease* may still be acceptable for transplantation such as those with a bicuspid aortic valve and those with myxo-

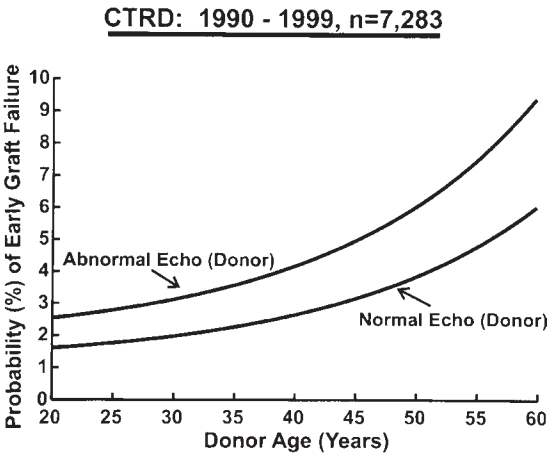


FIGURE 5.7. Nomogram from Cardiac Transplant Research Database (CTRD) multivariable analysis depicting the effect of donor age and left ventricular function by echocardiography (echo) on fatal early graft failure. (Young et al.,[19] with permission).

matous degeneration of the mitral valve. Back table mitral valve repair has been reported as a satisfactory option for donor hearts with significant mitral regurgitation.[22]

Donor hearts with potential toxicity have been considered for transplantation. *Cocaine abuse* has direct effects on the heart, which include vasoconstriction, endothelial dysfunction, and myocardial toxicity. These effects have been principally related to the intravenous use of cocaine, and hearts from donors with intravenous cocaine abuse are currently not suitable for transplantation. However, donors with a history of nonintravenous cocaine abuse who have normal left ventricular systolic function with no evidence of left ventricular hypertrophy are currently considered suitable.[22]

There are direct toxic effects of *alcohol* on the myocardium and recipients who have received hearts from donors with a history of significant alcohol abuse have inferior survival. Hence, if a strong history of chronic alcohol abuse can be elicited, hearts from these donors should not be used for cardiac transplantation.[23] Use of hearts from donors dying from *carbon monoxide poisoning* is still contentious. However, use of hearts from such donors is probably safe, provided the electrocardiogram and echocardiogram are normal with minimal elevation of cardiac enzymes, and minimal inotropic requirements.

Transplantation of hearts from hepatitis C positive donors to hepatitis C negative recipients is associated with substantially inferior survival and this strategy cannot be recommended. However, transplantation of hearts from hepatitis C positive donors to hepatitis C positive recipients can be considered.

Although supplying only a very small number of donor hearts, the *"domino procedure"* (the use of a heart from a heart/lung transplant recipient) appears to provide just as good survival as the use of cadaveric donors.[24]

5.3. Donor–Recipient Matching

The prevention of *donor–specific alloreactivity (lymphocytotoxic IgG antibodies against donor class I HLA antigens) in a potential recipient* is the goal of either prospective cross-matching at the time of identification of the donor, or detection of sensitization at the time of listing (prior pregnancy, blood transfusion, transplantation, or insertion of a ventricular assist device, VAD). In the case of sensitization, a prospective cross-match would be required. Controversy still exists regarding the presence of a T-cell negative/B-cell positive cross-match, although available evidence would suggest that under those circumstances these patients require augmented immunosuppression with cytolytic therapy (and/or IL-2 receptor blockade) and close surveillance for acute cardiac rejection. The role of desensitization preoperatively is also not universally accepted.

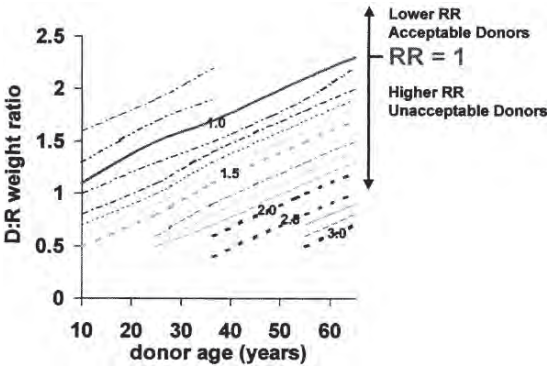


FIGURE 5.8. Iso-risk curves plot, based on donor age and donor:recipient weight ratio, for patients on the intensive care unit before transplant. DR, donor:recipient; RR, relative risk. (DeMeester et al.,[25] with permission).

Donor–recipient size matching should not be considered in isolation from other factors such as donor age and acuity of the transplant procedure. The use of hearts from donors whose body weight is no greater than 30% below that of the recipient is generally considered safe,[22] but undersizing with older donors age is clearly associated with an increasing risk[25] (Figure 5.8), and certainly this information would argue against the use of small donor hearts from an older donor to "rescue" a critically ill recipient.

5.4. Cardiac Transplant Procedure

5.4.1. Myocardial Preservation

Myocardial preservation during cardiac transplantation is vitally important. Biochemical derangements induced during the ischemic process may contribute

DropBooks

to primary graft failure, and preservation strategies that improve posttransplant graft function may allow longer ischemic times and the use of marginal donor hearts, with greater confidence that posttransplant function will be satisfactory. Biochemical processes involved in myocardial preservation are complex, but the primary methods of achieving cellular and functional integrity of the myocardium are through hypothermia and mechanical arrest of the heart. According to van't Hoff's law, which relates the rate of a chemical reaction to temperature, in mammalian enzyme systems there is an approximately 50% reduction in myocardial enzymatic reactions for every 10°C decline in cardiac temperature, which decreases but does not eliminate cellular activity completely.[26] Even though the heart is mechanically arrested, ATP is still being consumed at a low level to allow breaking of actin–myosin cross-bridges. If ATP depletion continues below a threshold level, irreversible contracture will occur. Although the myocardium can use stored glycogen to produce ATP by anaerobic glycolysis to maintain an ATP level above the critical threshold, once contracture commences ATP consumption markedly increases. The maintenance of ion homeostasis is also an important requirement of preservation. Even though with hypothermia Na^+ -K^+ ATPase activity is markedly reduced, passive ion movement will still occur down a concentration gradient. As a result, intracellular H^+ ions are exchanged for extracellular Na^+ ions and Ca^{2+} is also exchanged for Na^+. This produces an increased intracellular solute accumulation with water entering the cell down an osmotic gradient, and this intracellular edema may result in disruption of structural integrity. It is the accumulation of Ca^{2+} in the cytoplasm that may on reperfusion result in hypercontracture.[27]

Preservation solutions are distinguished by their ionic composition as either "extracellular" or "intracellular." The clinical results of UW solution (an intracellular solution) demonstrate excellent myocardial preservation out to approximately 6 h. UW solution also contains oxygen-derived free-radical scavenger molecules in an endeavor to ameliorate the ischemia/reperfusion injury that may be in part related to oxygen-derived free radical production. Preservation solutions may contain a variety of agents including impermeants (such as raffinose and lactobionate) and oncotic molecules (such as hydroxyethyl starch), metabolic substrates as well as molecules that inhibit the consumption of ATP and inhibit the Na^+ -H^+ exchanger, and Mg^{2+} as a Ca^{2+} antagonist.[28]

5.4.2. Technique of Orthotopic Cardiac Transplantation

The biatrial orthotopic cardiac transplant procedure that was developed by Lower and Shumway[29] remained unchanged for approximately 30 years. However, the bicaval orthotopic technique[30–32] is now the recommended technique since tricuspid incompetence and abnormal atrial contribution to ventricular filling may be reduced. There is also emerging evidence of having dynamic and electrochemical superiority of the total technique. The donor heart procurement procedure involves an incision in the left atrium to decompress the left ventricle and division of the inferior vena cava to decompress the heart, cross-clamping of the ascending aorta, and commencement of the infusion of preservation solution together with topical cooling. The heart is excised by transecting the inferior vena cava, superior vena cava (at the confluence of the innominate and right interval jugular vein), ascending aorta, and the main pulmonary artery (or pulmonary artery branches if the lungs are not being procured), and transaction of the left atrium above the atrioventricular groove (or pulmonary veins if the lungs are not being procured) (Figure 5.9). The heart is triple bagged with preservation solution and ice slush. In the recipient operating room a median sternotomy is performed and cardiopulmonary bypass is established with separate caval cannulation. Following aortic cross-clamping and snaring of the caval tapes, cardiectomy is performed by entering the left atrium anterior to the right pulmonary veins and carrying this incision superiorly and inferiorly under the caval. The right atrium is divided well above the right atrial–inferior vena cava junction and also on the atrial side of the superior vena caval–right atrial junction. The ascending aorta and main pulmonary artery are divided (Figure 5.10).

Prophylactic tricuspid annuloplasty of the donor heart prior to implantation was shown by Jeevanandam and coworkers to be effective in improving short-term mortality and long-term renal function.[33]

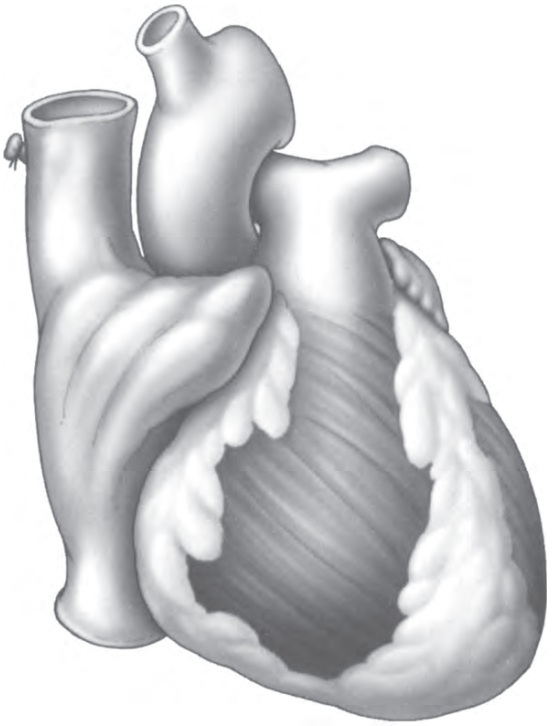


FIGURE 5.9. Completed excision of donor heart. Additional length of superior vena cava has been obtained in preparation for a bicaval implantation. (Kirklin et al.,[22] with permission).



FIGURE 5.10. Division of the right atrium to create superior and inferior vena cava cuffs for bicaval technique. The great vessels are divided as in the standard orthotopic method. (Kirklin et al.,[22] with permission).

5.4.2.1. Total Technique

The left pulmonary vein cuffs are first sutured together with 3–0 polypropylene. Prior to this, the posterior left atrial wall of the recipient is visualized and divided vertically between left and right pulmonary vein orifices. The left and right pulmonary vein orifices are mobilized as cuffs. The donor left atrium is also appropriately tailored to fashion pulmonary vein cuffs. The left cuff is followed by the right pulmonary vein cuff. Before this anastomosis is complete, a vent is placed to prevent left ventricular distension. This is followed by anastomoses of the IVC, SVC, main pulmonary artery, and aorta in sequence. This technique is usually possible when both lungs have not been harvested (Figure 5.11A and B).

5.4.2.2. BiCaval Technique

The left atrial anastomosis is constructed using 3–0 polypropylene as for biatrial orthotopic cardiac transplantation (Figure 5.11C). The inferior vena cava anastomosis is performed with continuous 4–0 polypropylene and the superior vena caval anastomosis is performed with continuous 5–0 polypropylene. The pulmonary artery anastomosis is then performed with continuous 5–0 polypropylene following which the aortic anastomosis is performed with continuous 3–0 polypropylene (Figure 5.12). Following deairing the aortic cross-clamp is removed from the heart and reperfused. An alternative sequence is to perform both the superior vena cava and pulmonary artery anastomoses following cross-clamp removal with the heart in a beating, perfused state. When rewarming is complete and cardiac function is satisfactory, the patient is weaned from cardiopulmonary bypass.

5.5. Posttransplant Immunosuppression

Acute “cellular” cardiac rejection is mediated by T-cell activation and to mitigate against this powerful response, a variety of immunosuppressive drugs are available. In order to minimize the toxicity of higher doses of individual agents and benefit from the synergy of multiple drugs, these agents are used in combination at lower doses, targeting complementary pathways of T-cell activation (Figure 5.13).

DropBooks

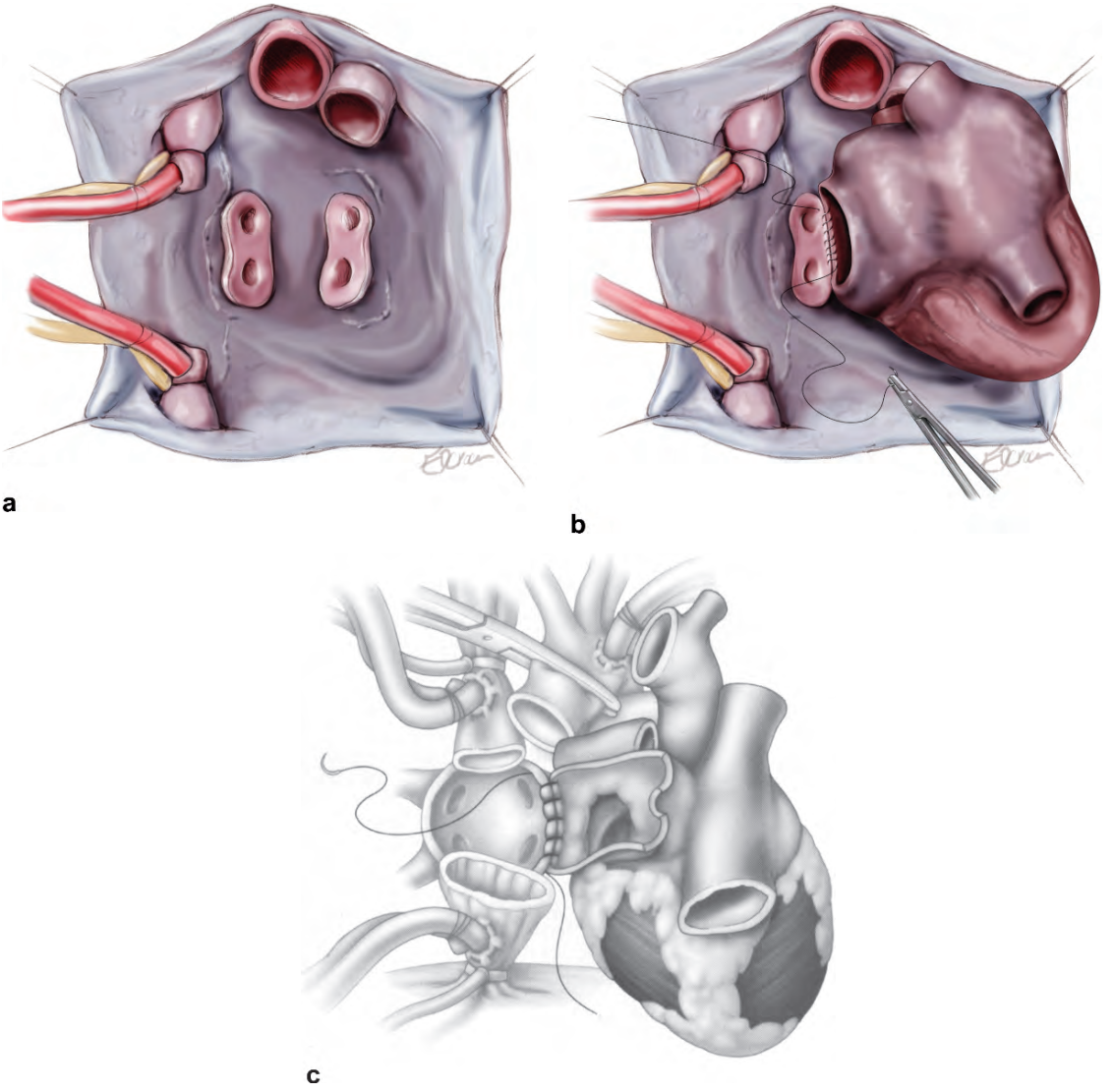


FIGURE 5.11. **A** The technique of a total transplant, with the recipient shown after donor cardiectomy. **B** The steps of a total transplant, showing the right pulmonary vein cuff being anastomosed. The left pulmonary vein cuff has already been completed. **C** Commencement of left atrial anastomosis in the bicaval technique (same as for biatrial orthotopic cardiac transplantation). (Kirklin et al.,[22] with permission).

5.5.1. Immunosuppression Modalities

Corticosteroids have a long history in transplant immunosuppression and are still regarded as an essential component of the perioperative and postoperative immunosuppression protocol in cardiac transplantation. The benefit of corticosteroids is based on both their immunosuppressive and anti-inflammatory properties. The quite nonspecific immunosuppression properties of steroids relate to their effect at a number of levels of T-cell activation, including suppression of antigen presentation to the T-cell and suppression of gene transcription in the nucleus to inhibit the expression cytokine such as interleukin-2 (IL-2) as well as a number of other cytokines. Corticosteroids also suppress macrophage function and B-cell proliferation, inhibit transmigration of leukocytes through blood vessels and reduce adhesion molecule expression. The anti-inflammatory properties of corticosteroids are

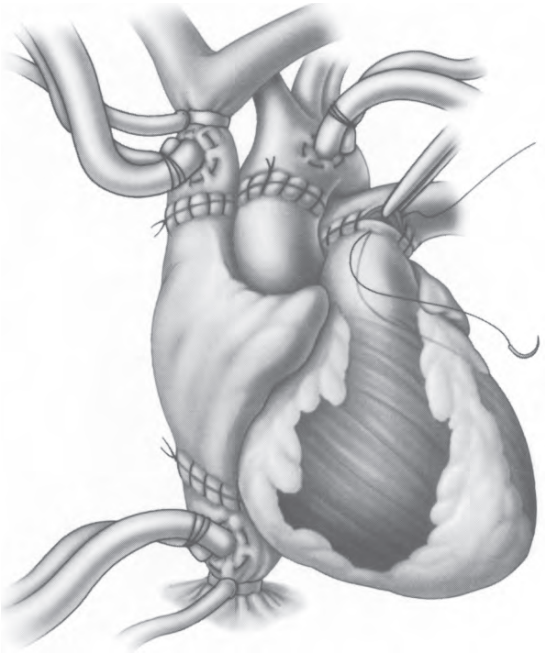


FIGURE 5.12. Completion of bicaval transplant technique, showing the inferior vena cava, superior vena cava, aortic and pulmonary artery anastomoses. (Kirklin et al.,[22] with permission).

DropBooks

due to inhibition of inflammatory mediators such as leukotrienes and prostaglandins and, probably through this mechanism, promote rapid reversal of symptoms of clinical rejection. However, it is the toxicity of corticosteroids that is responsible for much of the morbidity associated with immunosuppression, such as diabetes, obesity, impaired wound healing, avascular necrosis of the femoral head and osteoporosis, cataracts, pancreatitis, and gastrointestinal complications such as peptic ulcer disease and colonic perforation.[22] Because of this important toxicity, eliminating corticosteroids from the immunosuppression protocol is a goal that has been variably achieved. Patients most likely to benefit from steroid-free immunosuppression are pediatric cardiac transplant patients, postmenopausal females, and patients with severe osteoporosis, insulin-dependent diabetes, and marked obesity.[22] Withdrawal of steroids without incurring recurrent rejection during the first 30 days after transplantation can be achieved in approximately 40–60% of patients.[35–37] After 3 months, successful withdrawal of steroids can be expected in 60–90% of recipients.[38,39] Successful withdrawal is less likely to occur in patients with prior rejection history and in women.

The availability of *calcineurin inhibitor*–based immunosuppression *(cyclosporine or tacrolimus)* was one of the advances that marked the turning point in cardiac transplantation from an era of poor results to one of a mature effective therapy. The mechanism of action of cyclosporine is blockade of the calcineurin pathway, hence blocking the transcription of IL-2 and other cytokines. Cyclosporine, however, is associated with a number of toxic effects, including nephrotoxicity, hypertension, hepatotoxocity, neurologic problems including hand tremors and seizures, gingival hyperplasia, and hypertrichosis. The nephrotoxicity may manifest early after transplantation and appears to be mediated through renal arteriolar vasoconstriction. Chronic cyclosporine nephrotoxicity, which is associated with prolonged use of the drug, is characterized by patchy glomerular sclerosis and interstitial fibrosis within the renal parenchyma. The original cyclosporine formulation was oil based and its gastrointestinal absorption was rather variable. The development of a microemulsion formulation of cyclosporine has reduced the variability in absorption with more reliable blood levels. Tacrolimus inhibits T-cell activation and proliferation through the blockade of calcineurin, but by a mechanism entirely different from that of cyclosporine. The place of tacrolimus was initially as “rescue therapy” for cardiac transplant patients with resistant rejection but is now frequently used as a primary agent. The toxicity of tacrolimus includes nephrotoxicity (although there is some evidence that it may be less nephrotoxic than cyclosporine), neurologic side effects including tremor, headache, confusion (which are dose related), glucose intolerance, and hyperkalemia. There is some evidence that hypertension may be less prevalent than with cyclosporine. Although some centers are using tacrolimus as primary therapy, it is most commonly used to replace cyclosporine following recurrent rejection or because of cyclosporine toxicity.

Azathioprine has been a component of immunosuppression since the earliest days of transplantation. It is a purine analogue which inhibits purine synthesis and therefore interferes with DNA and RNA synthesis, consequently suppressing T- and B-cell proliferation. The most important toxicity of azathioprine is myelosuppression,

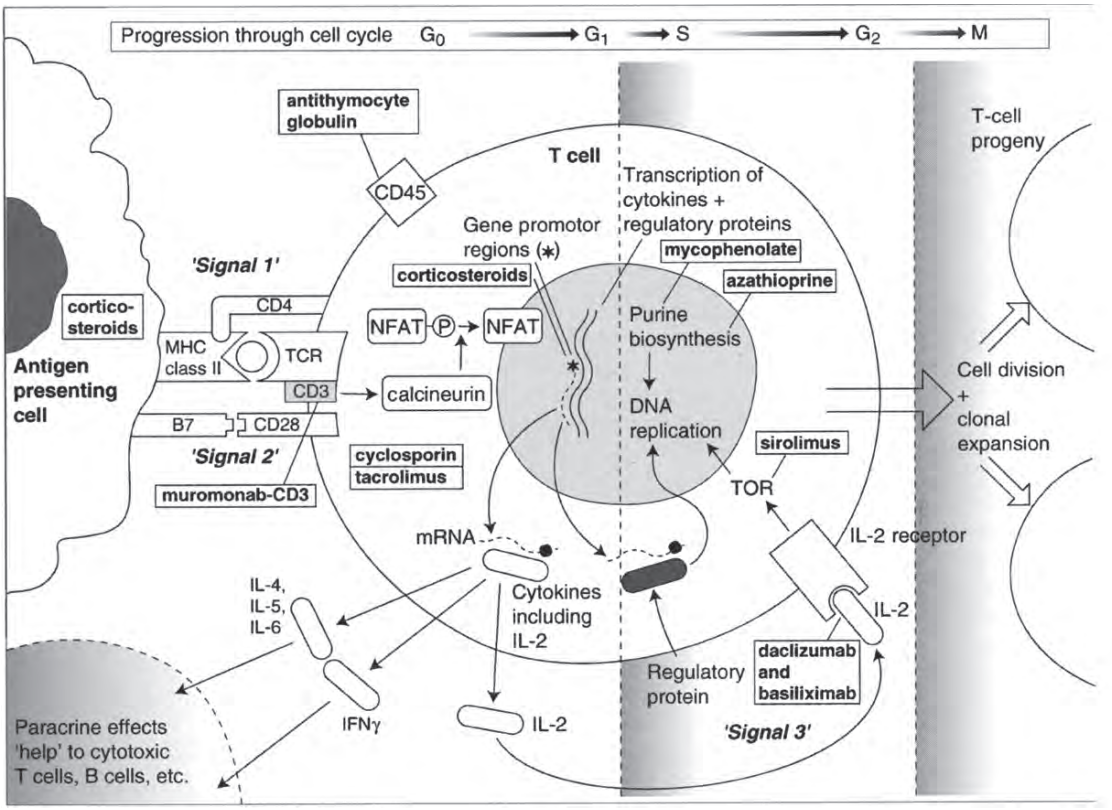


FIGURE 5.13. Simplified model of the events that occur during T-cell activation. The sites of action of each of the immunosuppressive agents discussed in this chapter are shown. Polyclonal antithymocyte globulin is shown as binding to the common leukocyte antigen but, in reality, contains antibodies which bind to many different T-cell antigens. NFAT, nuclear factor of activated T-cells, TCR, T-cell receptor, MHC, major histocompatibility complex; P, phosphate, CD, cluster of differentiation antigen; TOR, target of rapamycin; IL, interleukin; IFN-γ, interferon gamma. (Banner et al.,[34] with permission).

which is dose dependent. Other toxicity includes hepatotoxicity and pancreatitis. Azathioprine may also predispose to malignant transformation, particularly development of cutaneous squamous cell carcinoma.

Mycophenolate mofetil (MMF) inhibits the *de novo* purine synthesis pathway and since human lymphocytes are able to synthesize purine DNA only through the *de novo* pathway, they are particularly susceptible to the action of this drug. As a result, MMF inhibits the proliferation of both T- and B-cells. The most frequent toxicity of MMF is gastrointestinal, including nausea, vomiting, and diarrhea, which although normally responds to a gradual increase in the dose, may be severe enough to require discontinuation. Although evidence for the superiority of immunosuppression provided by MMF compared to azathioprine is sparse, the suggestion that MMF may result in lower mortality (decreased rejection and incidence of rejection and infection) and reduction in the incidence of grade 3A or greater rejection and the requirement for rejection treatment[40] has resulted in MMF increasingly replacing azathioprine as primary immunosuppression.

Anti-lymphocyte globulins were originally developed for use as induction therapy. Polyclonal antibodies are produced by inoculation of animals with human lymphocytes, thymocytes, and lymphoblasts, and hence their mechanism of action is directed against a number of T-cell molecules as well as B-cells. There may also be antibodies

in the preparation that react against monocytes, macrophages, platelets, and neutrophils. On the other hand, monoclonal antibody preparations are directed against a specific cell surface molecule or they can block a specific receptor ligand and hence have the advantage of specificity. For example, OKT3 is directed against CD3 antigen and campath is directed against the CD52 antigen. Both monoclonal and polyclonal antibodies are associated with an increased risk of viral infection (particularly cytomegalovirus, CMV) due to suppression of cell-mediated immunity against viruses. They are also associated with the development of post-transplant lymphoproliferative disorder (PTLD) as a result of reactivation of latent Epstein-Barr virus (EBV), which can induce transformation of an EBV-dependent polyclonal B-cell population into a malignant monoclonal B-cell lymphoma. Although OKT3 was widely used as "induction therapy," there is no consistent evidence that the use of induction therapy improves survival except in patients at high risk for rejection.[41] Therefore, the use of antilymphocyte antibody therapy is now usually limited to specific situations: (1) to delay the introduction of cyclosporine immediately after transplantation because of nephrotoxicity or hepatotoxicity, (2) in patients at increased risk of rejection because of sensitization or a positive B-cell cross-match, and (3) treatment of recurrent or persistent rejection that is not responsive to pulse steroid therapy.

IL-2 receptor inhibition (anti-CD25) is mediated by a monoclonal antibody that binds to the CD25 molecule which is present on activated (but not resting) T-cells. Basiliximab is a chimeric antibody that still retains some of the murine components of the immunoglobulin chain whereas daclizumab is a humanized antibody. The current role of IL-2 receptor blockade has not been completely clarified, but there is evidence in renal transplantation[42] of reduction in the number of rejection episodes and an increase in the time to first rejection without an increase in the incidence of infection or malignancy. Studies in cardiac transplantation[43] suggest that time to first rejection is increased, and that overall rejection severity is decreased with induction daclizumab therapy. Interestingly, following cessation of therapy, rejection frequency rebounds. IL-2 receptor blockade is being increasingly used as induction therapy, but any benefits of this policy have yet to be determined.

The *target of rapamycin (TOR) inhibitors* are drugs that block the proliferation signals that connect the autocrine stimulation by IL-2 on the cell surface to the cell nucleus for proliferation of T-cells. These antiproliferative effects are limited to T- and B-cells, but these drugs also have antiproliferative effects on mesenchymal cells such as fibroblasts. The toxicity of sirolimus includes renal dysfunction (when combined with cyclosporine), hypertension, hyperlipidemia, and thrombocytopenia. In addition, a particularly concerning side effect that has emerged is delayed wound healing, and for that reason these drugs should probably not be used in the first 3 months after transplantation. The role of these agents in cardiac transplantation has not been clarified, but sirolimus may reduce the incidence of acute graft rejection and refractory acute graft rejection.[43] The use of sirolimus or everolimus may reduce the incidence of coronary allograft vasculopathy and the rate of progression in patients with already established coronary allograft vasculopathy.[44–45] The current role of TOR inhibitors is under evaluation, but it may be a useful drug as a substitute for cyclosporine or tacrolimus in patients with calcineurin inhibitor induced nephrotoxicity.

Plasmapheresis is separation of plasma and hence removal of large macromolecules from the blood including antibodies. Plasmapheresis is used in patients with rejection associated with donor-specific antibodies, a positive cross-match, and evidence of humoral rejection, and for patients with hemodynamically compromising rejection.

Photopheresis is an immunomodulatory therapy that is effective in the treatment of cutaneous T-cell lymphoma and scleroderma. This therapy involves separation of leukocytes, exposure of these leukocytes to a photoactivatable compound (8-methoxypsoralen), and irradiation by ultraviolet light, inhibiting DNA replication. The precise mechanism of its immunosuppressive effect is not known, but it is probably more complex than just damaging target cells, and may include induction of a suppressor T-cell response. Photopheresis is most commonly employed in cardiac transplantation as an adjunct therapy for patients with recalcitrant rejection or following reversal of an episode of hemodynamic compromising rejection to prevent recurrence.

DropBooks

Immunosuppression at UAB involves preoperative MMF and corticosteroids, intraoperative corticosteroids and basilixamab, and postoperative corticosteroids (intravenous followed by maintenance prednisone), MMF, tacrolimus, and basiliximab (postoperative day 4).

5.6. Acute Cardiac Rejection

The risk of acute cardiac rejection has a well-defined time pattern (Figure 5.14) with the risk being highest within the first 3 months after transplantation, then falling to a low level at approximately 6 months after transplantation, although the risk of acute rejection never completely disappears. This time course dictates that immunosuppression and the surveillance for acute rejection should be intensified in the first 6 months after transplantation and thereafter may be reduced, although surveillance should never be completely eliminated. Most patients with acute cardiac rejection are asymptomatic, and it is detected on routine endomyocardial biopsy. By the time a patient becomes symptomatic with acute cardiac rejection, the injury to the myocardium from the rejection process may be quite advanced. Many noninvasive tests (biochemical, immunological, electrophysiological, nuclear, and functional) have been investigated and none (or any in combination) have sufficient sensitivity to be considered as a screening test for acute cardiac rejection. The gold standard is endomyocardial biopsy. The endomyocardial biopsy grading has been standardized by the International Society for Heart and Lung Transplantation (ISHLT) and is outlined in Table 5.6. This system grades rejection from grade 0 (no rejection) to grade 4 (severe acute rejection), although simplification of this system has been recommended with categorization into mild, moderate, and severe groups. Grade 1A (Figure 5.15) is a focal perivascular infiltrate predominately of lymphocytes without any injury to the myocyte. Grade 1B (Figure 5.16) is a lymphocytic infiltrate that is predominately interstitial with mononuclear cells and without myocyte injury. Grade 2 (Figure 5.17) is a single focus of a mononuclear infiltrate which has a more aggressive picture that does involve myocyte injury. Grade 3A rejection (Figure 5.18) is a similar pattern to grade 2 rejection except that it involves two or more foci, but the intervening myocardium is

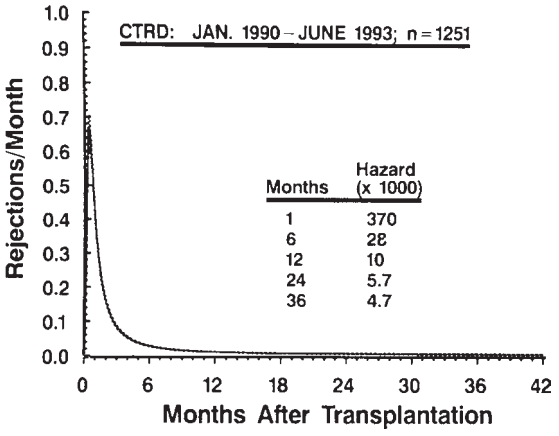


FIGURE 5.14. Hazard function for initial rejection episode after heart transplantation. Dashed lines indicate the enclosed 70% confidence limits. *CTRD*, Cardiac Transplant Research Database. (Kubo et al.,[46] with permission).

TABLE 5.6. ISHLT standardized endomyocardial biopsy grading scheme.

Grade	Description	Nomenclature
0	No lymphocyte infiltrate	No rejection
1A	Focal (perivascular or interstitial) lymphocytic infiltrate without myocyte necrosis	Focal mild acute rejection
1B	Diffuse but sparse lymphocytic infiltrate without myocyte necrosis	Diffuse mild acute rejection
2	One focus only with "aggressive" lymphocytic infiltrate and/or focal myocyte injury	Focal moderate acute rejection
3A	Multifocal aggressive lymphocytic infiltratrates and/or myocyte necrosis	Multifocal moderate acute rejection
3B	Diffuse, inflammatory process with myocyte necrosis	Diffuse borderline severe acute rejection
4	Diffuse, aggressive, polymorphous infiltrate with necrosis (± edema; ± hemorrhage; ± vasculitis)	Severe acute rejection

Billingham,[47] with permission.
ISHLT International Society for Heart and Lung Transplantation.

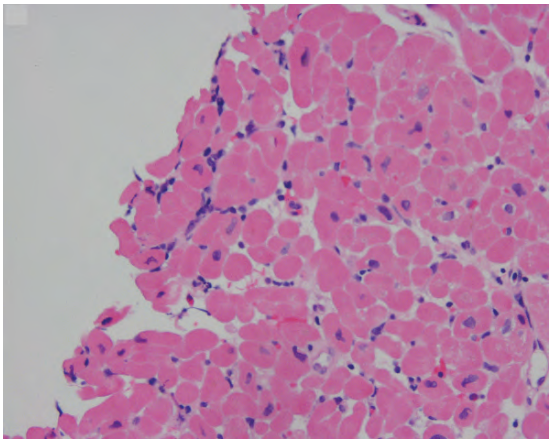


FIGURE 5.15. Grade 1A.

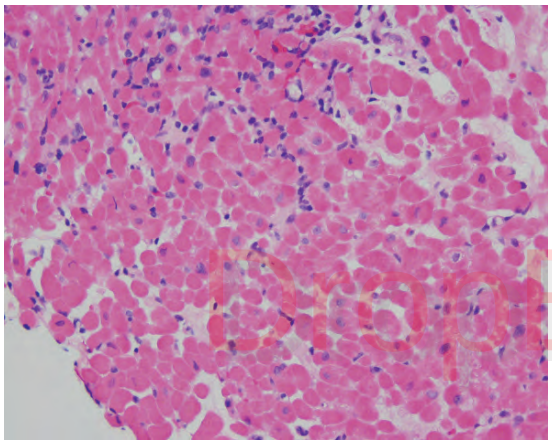


FIGURE 5.16. Grade 1B.

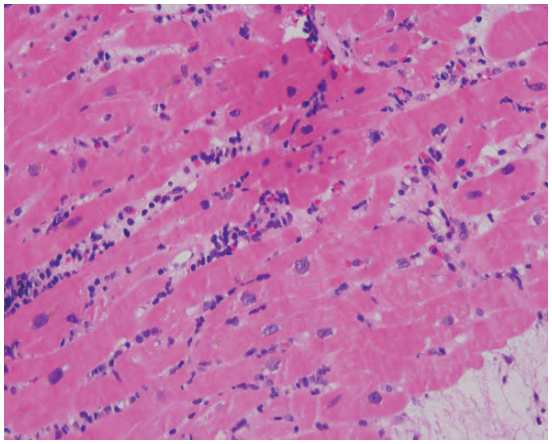


FIGURE 5.17. Grade 2.

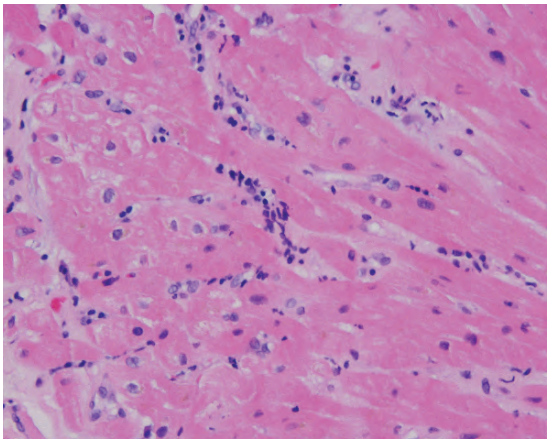


FIGURE 5.18. Grade 3A.

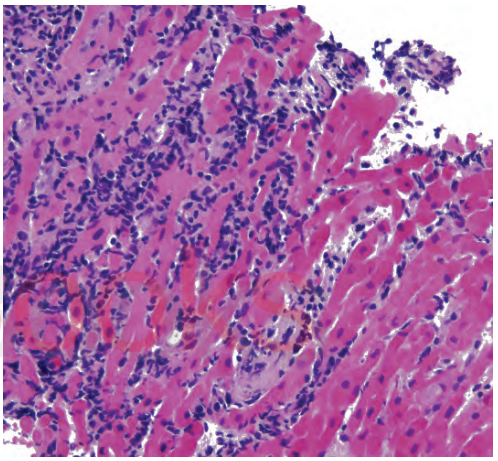


FIGURE 5.19 Grade 3B.

normal. Grade 3B rejection (Figure 5.19) is a diffuse mononuclear infiltrative process with myocyte injury and compared with grade 3A rejection, the infiltrate is more diffuse with little intervening normal myocardium. Grade 4 rejection, which is rarely seen, is the most severe form of acute rejection. It is characterized by widespread injury, edema, hemorrhage, and a polymorphous inflammatory infiltrate.[48]

The treatment of acute or persistent cardiac rejection varies between programs. However, the general principles are the following. Mild and moderate grades of rejection are treated with intravenous pulse corticosteroids within the first 6 months after transplantation or oral prednisone

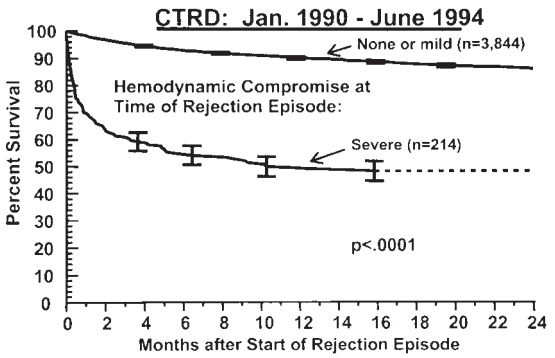


FIGURE 5.20. Actuarial survival after rejection episode. Upper curve indicates rejection with no or mild hemodynamic compromise, and lower curve rejection with severe hemodynamic compromise. Error bars enclose 70% confidence limits. (Mills et al.,[49] with permission).

(beyond 6 months after transplantation). Higher grades of rejection (such as grade 3A or greater), if occurring early after transplantation, are treated with intravenous corticosteroids together with cytolytic therapy. Persistent high-grade rejection may also require consideration of other strategies such as augmentation of baseline immunosuppression, photopheresis, or addition of another agent such as sirolimus. Acute cardiac rejection with hemodynamic compromise is an uncommon but potentially lethal process. Patients can present with low cardiac output or decreased ejection fraction by echocardiography, and the treatment involves inotropic agents, plasmapheresis, cytolytic therapy, and corticosteroids. Once a patient has an episode of hemodynamic compromising rejection, the mortality is approximately 50% within the next 12 months (Figure 5.20). This argues for prolonged augmented immunosuppression, close surveillance with frequent endomyocardial biopsies, and the use of photopheresis to protect against the high likelihood of further episodes of hemodynamically compromising rejection.

5.7. Infection

The prevention and management of infection constitutes a significant part of the workload after transplantation[50]: A broad range of organisms may be involved including the usual pathogenic organisms, as well as organisms that are not normally pathogenic except in immunocompromised hosts, endogenous organisms, and donor-transmitted infectious disease organisms. Presentation of infectious disease in immunocompromised patients may be quite different from that in non-immunocompromised patients with blunting of signs and symptoms because of the effect of immunosuppression on the inflammatory response. Infection may indirectly injure the transplanted heart through immune modulation (coronary allograft vasculopathy) or cause malignant transformation (EBV). Infection and rejection may coexist since treatment of rejection may precipitate infectious complications and certain immunomodulating viruses may precipitate rejection.

The term “immunocompromised host” refers to patients where host defenses are impaired because of immunosuppression. These patients are susceptible to infection caused by[51] true pathogens (organisms that are able to overwhelm the natural defense mechanism of an non-immunocompromised host), pathogens which may colonize a mucocutaneous surface and cause infection when there is a breach in that surface, and nonpathogens that do not present a risk to a normal host, but to which immunocompromised patients are susceptible. The term opportunistic infection refers to infection in immunocompromised patients that may be caused by true pathogens, nonpathogens, or sometime pathogens that may produce an illness that clinically may be quite different from that produced in a host with normal defense mechanisms.[51]

Normal host defense mechanisms are usually highly successful in minimizing the risk of infectious disease. The first line of defense is epithelial/mucosal barriers that defend against micobiological penetration.[52] The skin, epithelial surface of the lung, and mucosal surface of the gastrointestinal tract are surfaces that can be readily breached and represent portals of micobiological entry and invasion after cardiac transplantation. Immunological mechanisms are the second line of defense and the components are humoral, cellular, and phagocytic. All of these components may be seriously compromised by the variety of immunosuppressive modalities that may be used after cardiac transplantation.

The susceptibility to infection of a patient after heart transplantation is a function of a complex interplay of multiple factors which contribute to

the "net state of immunosuppression."[53] These factors include recipient comorbid disease such as diabetes, malnutrition, hepatic dysfunction, renal dysfunction, age, the nature and dose of immunosuppressive agents, compromise of the epithelial and mucosal defenses, and the presence of infection with immunomodulatory viruses, such as CMV and EBV. Immunosuppressive agents contribute in a major way to the development of infection. Corticosteroids increase susceptibility in infection through a number of mechanisms (both immunosuppressive and anti-inflammatory), including reduced accumulation of neutrophils at the site of inflammation, impairment of the mononuclear-phagocytic system, blunting of the T-cell activation cascade, inhibiting the function of alveolar macrophages, and impairment of wound healing. Cytolytic therapy, due to its effect of depleting circulating lymphocytes, is associated with an increased incidence of CMV infection and PTLD through EBV infection. Azathioprine reduces antibody production (by inhibiting B-cells), decreases cytotoxic T-cell proliferation, and impairs natural killer cell activity. Cyclosporine predisposes to infection through its blocking action on antigen-induced T-cell expression, although the risk of infection is less likely than with azathioprine/prednisone-based immunosuppression.

Infection has a predictable time-related probability (Figure 5.21), being highest in the first month after transplantation at a time when immunosuppression is at its most intense, when epithelial and mucosal barriers are at their most vulnerable because of surgical wounds and instrumentation. The time course for different infectious agents after cardiac transplantation is quite distinct[55] (Figure 5.22).

From a numerical perspective, CMV infection is the most important infection after cardiac transplantation. As a member of the herpesvirus family, CMV has the characteristic of latency and hence CMV infection may occur by transmission from donor to recipient (primary infection), or a recipient who is a reservoir of CMV because of previous infection may develop reactivation infection following commencement of immunosuppression following transplantation. The term reinfection (superinfection) is used when a CMV seropositive recipient receives a heart from a seropositive donor with a CMV strain that is different from the recipient latent CMV strain.

CMV has a number of direct and indirect effects. The direct effects include (1) CMV syndrome (a flu-like illness with fever, chills, malaise, leukopenia, and thrombocytopenia accompanied by CMV viremia), (2) CMV disease (CMV syndrome or tissue invasive disease accompanied by detection of CMV in tissue), (3) CMV infection (asymptomatic viremia, CMV syndrome, and CMV disease).

There are a number of potential indirect effects of CMV after cardiac transplantation. CMV infection, either symptomatic or asymptomatic, has been implicated in the pathogenesis of coronary allograft vasculopathy.[56–58] Asymptomatic CMV reactivation has been linked with the development of acute allograft rejection.[59] One study has

DropBooks

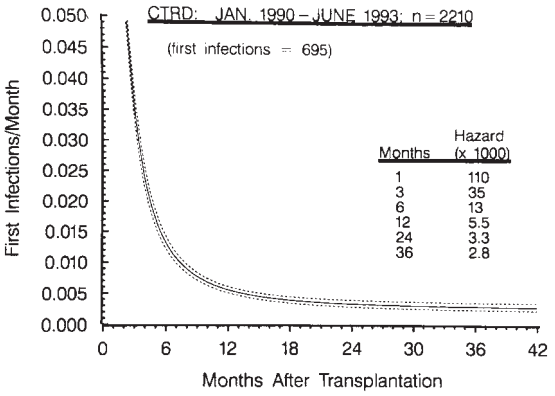


FIGURE 5.21. Hazard function for initial infection. Dashed lines represent the 70% confidence limits. *CTRD*, Cardiac Transplant Research Database. (Smart et al.,[54] with permission).

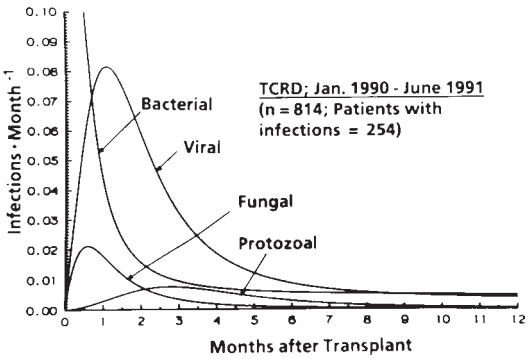


FIGURE 5.22. Hazard function (instantaneous risk over time) for first infection of each major category of infectious agent. *TCRD*, Transplant Cardiologist Research Database. (Miller et al.,[55] with permission).

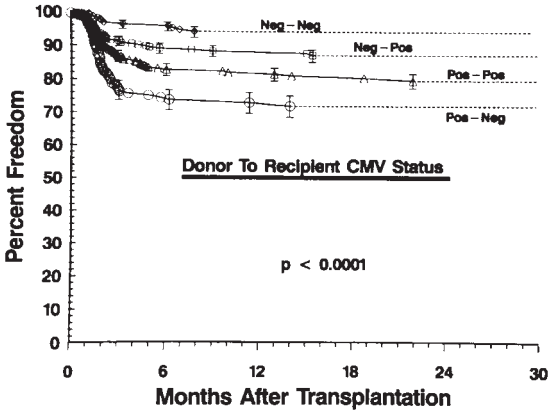


FIGURE 5.23. Actuarial freedom from initial Cytomegalovirus (CMV) infection according to CMV serologic status of donor and recipient before transplantation. Dashed lines indicate duration of follow-up. Error bars indicate ± 1 standard error. (Kirklin et al.)[22]

reported an association between asymptomatic CMV infection and higher rejection scores.[60]

The most important factor that determines the occurrence of CMV infection and disease after cardiac transplantation is the serological status of the donor and recipient, the highest risk being in CMV-negative recipients receiving hearts from CMV-positive donors[61] (Figure 5.23).

The clinical manifestations of invasive disease depend on the organ involved and the type of infection (patients with primary CMV infection as opposed to reactivation infection are more likely to be symptomatic with greater severity of symptoms). CMV infection can be highly variable, manifesting as gastritis, duodenitis, hemorrhagic colitis, retinitis, pneumonitis (a severe form of CMV disease that has a poor prognosis, more likely to occur in lung transplant patients), hepatitis (a rare event in cardiac transplant recipients), and encephalitis.

The standard treatment for CMV infection is ganciclovir, with strategies that include intravenous ganciclovir, oral valganciclovir, or sequential intravenous ganciclovir followed by valganciclovir. The duration of therapy varies considerably from 2 weeks to 6 months,[62] but there is evidence that therapy can be individualized as guided by the response to therapy (monitoring of the viral load). If CMV replication has been suppressed to a level that is undetectable, the risk of CMV disease relapse is low.[63]

Prevention of CMV infection is now the primary method employed to reduce its incidence, and two general strategies are used—prophylaxis and preemptive therapy. The most widely used strategy is universal prophylaxis (except for donor negative/recipient negative in most centers) and a variety of regimens are currently used including intravenous ganciclovir, valganciclovir, and a combination of CMV immune globulin and intravenous ganciclovir in the highest risk group. Preemptive therapy, which involves administration of anti-CMV treatment to patients who have objective evidence of CMV infection, does have the advantage that fewer patients are exposed to the risks of antiviral drugs. The effectiveness of this strategy is predicated upon accurate detection of the presence of CMV. The two most commonly used tests are pp65 antigenemia assay and molecular methods using polymerase chain reaction. The threshold for initiating preemptive therapy, particularly with molecular methods, remains controversial.

5.8. Coronary Allograft Vasculopathy

Coronary allograft vasculopathy is the manifestation of chronic cardiac rejection, and this process is one of the major factors limiting survival after cardiac transplantation. The fundamental morphology of the lesion of coronary allograft vasculopathy is progressive intimal thickening involving both epicardial and intramyocardial coronary arteries. One of the characteristics of this process is its diffuse nature and concentric obliterative lesions, which is distinct from typical atherosclerotic native CAD, that tends to produce focal, proximal, eccentric lesions, sparing intramyocardial branches.

A number of immunologic and nonimmunologic factors are believed to be responsible for coronary allograft vasculopathy. Donor/recipient immunological disparity, humoral rejection, repeated episodes, and higher grades of acute cardiac rejection likely predispose to this process. Nonimmunologic factors include the traditional atherosclerotic risk factors such as donor and recipient age, hypertension, smoking, hyperlipidemia, diabetes, and obesity, but additional factors may have a role. These include CMV infection (perhaps due to the impact

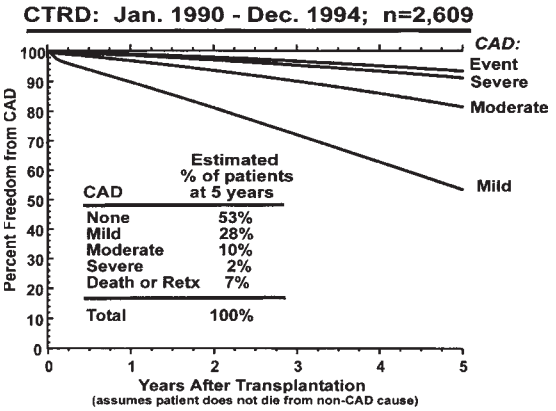


FIGURE 5.24. Actuarial (Kaplan-Meier) freedom from presence of mild (bottom line), moderate (middle line), or severe (top line) coronary artery disease (CAD) detected by coronary angiography performed later than 6 months after heart transplantation. A CAD event was defined as death or retransplantation due to coronary vasculopathy. (Costanzo et al.,[64] with permission).

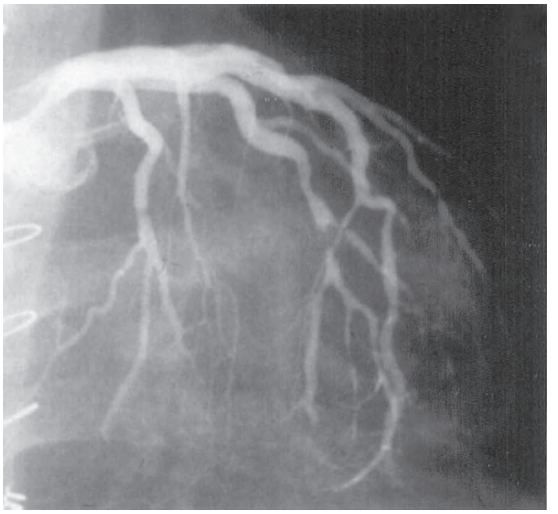


FIGURE 5.25. Coronary angiogram demonstrating severe allograft arteriopathy of large epicardial, smaller secondary branches, and distal vessels (note the abrupt cutoff of several arteries) in a patient who was 5 years posttransplant and died suddenly. (Kirklin et al.,[22] with permission).

of CMV on endothelial cells), impaired fibrinolysis, and ischemia/reperfusion injury at the time of the transplant.

The incidence of coronary allograft vasculopathy is substantial and by 5 years after transplantation 50% of patients have at least mild coronary allograft vasculopathy (Figure 5.24). However, severe coronary allograft vasculopathy accompanied by a coronary allograft vasculopathy event (death or retransplantation) is unusual within the first 5 years.

The standard method of diagnosing coronary allograft vasculopathy is by coronary angiography[22] (Figure 5.25) as part of the posttransplant surveillance protocol. Intracoronary ultrasound provides a more sensitive means of detecting coronary allograft vasculopathy because it actually images the arterial wall. Treatment of established coronary allograft vasculopathy is largely ineffective. Percutaneous intervention may offer some hope for focal stenoses, but for diffuse coronary allograft vasculopathy the only effective therapy is retransplantation. Prevention of the development and progression of coronary allograft vasculopathy is the focus of multiple treatment strategies. In addition to the usual strategies for control of typical atherosclerotic risk factors, additional measures that have shown some efficacy include calcium channel blockers, angiotensin-converting enzyme inhibitors, antiplatelet therapy, immunosuppressive agents with antiproliferative action (myocophenolate mofetil and sirolimus), photopheresis, and possibly anti-CMV therapy.

DropBooks

5.9. Malignancy

Malignancy after cardiac transplantation occurs in three major settings[22]: (1) transplantation in patients with preexisting malignancy, (2) transmission of a malignancy from donor to recipient, and (3) *de novo* malignancy developing in a recipient following cardiac transplantation. Malignancies most likely to occur in heart transplant patients are carcinomas of the lung, nonmelanoma skin cancers, lymphomas, carcinomas of the bladder, and pancreatic cancer.[65] However, defining a mandatory waiting time from treatment of the malignancy to cardiac transplantation that would ensure the lowest risk of recurrence has not proven possible and furthermore, an excessively long waiting time may result in a potential recipient dying from heart failure. Rarely, an unrecognized donor malignancy may be transmitted to a recipient. Potential mechanisms involved in the development

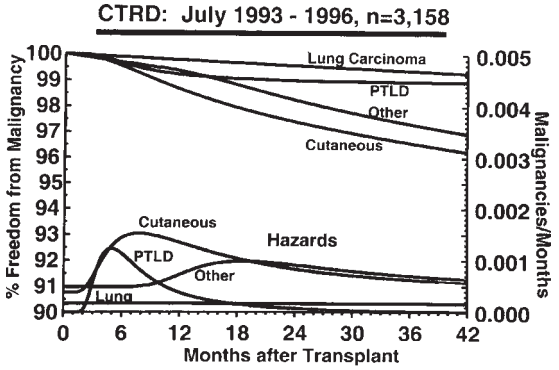


FIGURE 5.26. Parametric estimate of freedom from malignancy after heart transplantation for various malignancies and the respective hazard function. (DeSalvo et al.,[67] with permission).

of *de novo* recipient malignancy include disordered immune surveillance,[65] principally as a result of the burden of immunosuppression, and oncogenic viral infections caused by EBV (implicated in the development of PTLD which can transform into a malignant monoclonal line), herpes simplex virus, and human papillomavirus.

The incidence of malignancy after cardiac transplantation is approximately 3–4 times that of the general population.[66] Following cardiac transplantation there is a distinct pattern of malignancies (Figure 5.26), with the emergence of PTLD and cutaneous malignancy being most likely within the first 12–18 months after transplantation.

5.10. Other Long-Term Complications After Cardiac Transplantation

Numerous important long-term complications after cardiac transplantation may contribute to morbidity and mortality. Gastrointestinal complications include peptic ulcer disease (due to such causes as invasive CMV disease and *Helicobacter pylori* infection, and the use of corticosteroids), diverticular disease (perforation is likely increased by the use of corticosteroids), pancreatitis (due to invasive CMV disease, azathioprine toxicity, hyperlipidemia), and cholelithiasis. Ocular complications (cataracts and glaucoma both relate to corticosteroid use), hypertension, nephrotoxicity, hyperlipidemia, and bone complications (osteoporosis and avascular necrosis) assume increasing significance with improvement in posttransplant survival.

5.11. Survival After Cardiac Transplantation

The results of cardiac transplantation have progressively improved, and in the current era 10-year survival approaches 70% (Figure 5.27). The most common causes of death during the first year after cardiac transplantation[19] (Figure 5.28) are early graft failure, infection, acute cardiac rejection, and miscellaneous other causes (many reflecting critical illness). After the first year, the principal causes of death (Figure 5.29) are coronary allograft vasculopathy, malignancy, and additional causes, representing the appearance of complications of immunosuppression and other comorbid diseases.

Cardiac transplantation is a mature therapy for end-stage heart disease, but will always be constrained by the tremendous imbalance between the number of potential recipients and the number of available donor hearts. One of the challenges for

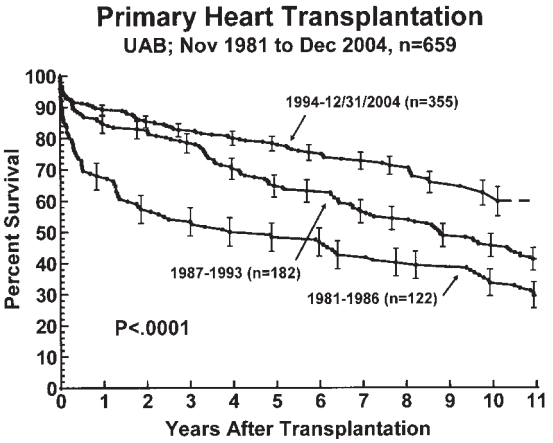


FIGURE 5.27. Actuarial survival following primary cardiac transplantation in three eras of the University of Alabama at Birmingham (UAB). The top actuarial curve depicts the years 1994–2004, the middle curve depicts the years 1987–1997, and the lower curve depicts the years 1981–1986. The vertical bars represent the 70% confidence limits.

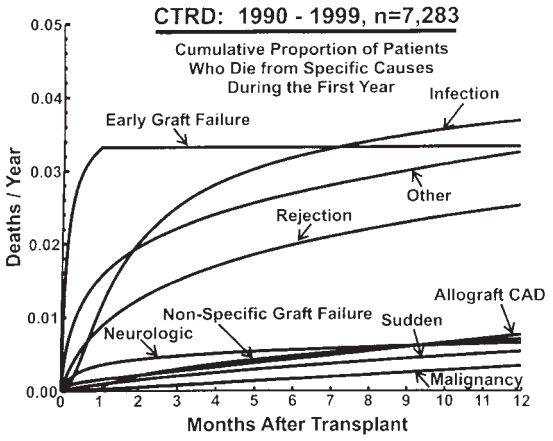


FIGURE 5.28. Competing outcomes analysis of specific causes of death during the first year after transplantation in the Cardiac Transplant Research Database. (Young et al.)[19]

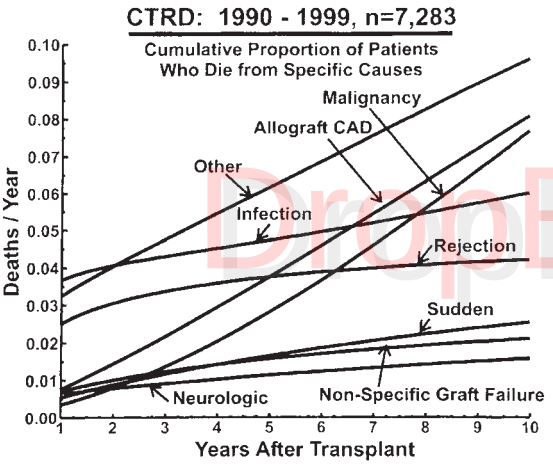


FIGURE 5.29. Competing outcomes analysis of specific causes of death during the first 10 years after transplantation in the Cardiac Transplant Research Database (CTRD). (Costanzo et al.)[68]

the future is to utilize the extraordinary amount of data that is available to classify patients with end-stage heart disease into those who are likely to experience the best results from cardiac transplantation and those who have risk factors that portend significantly inferior results (where other therapies such as chronic mechanical circulatory support may be an option). Only in this way will the assignment of appropriate therapy for patients in end-stage heart disease be rational.

Key Points to Remember

- Cardiac transplantation is established and a mature form of therapy which has become the gold-standard for the treatment of end-stage heart failure.
- Evaluation, selection and listing of patients for transplantation has to take into account many factors, including severity of heart failure, functional capacity, extent of medical therapy, indications for transplantation, etc.
- The timing of this therapy also has to be carefully tailored to each patient.
- While there are a few variations in the surgical technique, the overall principles of surgery remain the same.
- Peri-operatively, careful attention needs to immuno-suppression is mandatory, based on protocols, but individualized to patients according to various clinical parameters.
- Careful monitoring of patients is required post-operatively, with clinical reviews, regular endo-myocardial biopsies, right heart catheterization, etc.
- Life-long monitoring of transplant recipients is mandatory, because these patients walk a fine line between rejection and infection.

DropBooks

References

1. Kirklin J, McGiffin D, Pinderski L, et al. Selection of patients and techniques of heart transplantation. *Surg. Clin. North Am.* 2004;84(1):257-287.
2. Mancini D, Ronan N, Ascheim D, et al. Predictors of survival in patients with end-stage heart failure. *Circulation*. 2002;106:II680.
3. Aaronson K, Schwartz J, Chen T, et al. Development and prospective validation of a clinical index to predict survival in ambulatory patients referred for cardiac transplant evaluation. *Circulation*. 1997;95:2660-2667.
4. Jimenez J, Edwards L, Higgins R, et al. Should stable UNOS status 2 patients be transplanted? *J Heart Lung Transplant*. 2005;24:178-183.
5. Deng M, Smits J, Young J. Proposition: The benefit of cardiac transplantation in stable outpatients with heart failure should be tested in a randomized trial. *J Heart Lung Transplant*. 2003;22:113-117.
6. Kirklin J, Naftel D, Pearce F, et al. Should status II patients be removed from the pediatric heart trans-

plant waiting list: A multiinstitutional study. *J Heart Lung Transplant*. 2005;24(2S):64.
7. Radovancevic B, McGiffin D, Kobashigawa J, et al. Retransplantation in 7,290 primary transplant patients: A 10-year multiinstitutional study. *J Heart Lung Transplant*. 2003;22:862.
8. Boyle A, Colvin-Adams M. Recipient selection and management. *Semin Thorac Cardiovasc Surg*. 2004;16:358-363.
9. Takada M, Nadeau K, Hancock W, et al. Effects of explosive brain death on cytokine activation of peripheral organs in the rat. *Transplantation*. 1998;65:1533-1542.
10. Wilhelm M, Pratschke J, Beato F, et al. Activation of the heart by donor brain death accelerates acute rejection after transplantation. *Circulation*. 2000;102:2426-2433.
11. Szabo G. Physiologic changes after brain death. *J Heart Lung Transplant*. 2004;23:S223-S226.
12. Szabo' G, Hackert T, Sebening C, et al. Modulation of coronary perfusion pressure can reverse cardiac dysfunction after brain death. *Ann Thorac Surg*. 1999;67:18-26.
13. Klautz R, Teitel D, Steendijk P, et al. Interaction between afterload and contractility in the newborn heart. Evidence of homeometric autoregulation in the intact circulation. *J Am Coll Cardiol*. 1995;25:1428-1435.
14. Asanoi H, Ishizaka S, Kameyama T, et al. Neural modulation of ventriculoarterial coupling in conscious dogs. *Am J Physiol*. 1994;266:H741-H748.
15. Arnold G, Kosche F, Miessner E, et al. The importance of the perfusion pressure in the coronary arteries for the contractility and the oxygen consumption of the heart. *Pfügers Arch*. 1968;299:339-356.
16. Arnold G, Morgenstern C, Lochner W. The autoregulation of the heart work by the coronary perfusion pressure. *Pflügers Arch*. 1970;321:34-55.
17. Hosenpud J. Cardiac transplantation. In: Hosenpud J, Greenberg B eds. *Congestive Heart Failure*. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2000:785-807.
18. Young J, Naftel D, Bourge R, et al. Matching the heart donor and heart transplant recipient. Clues for successful expansion of the donor pool: A multivariable, multiinstitutional report. *J Heart Lung Transplant*. 1994;13:353-365.
19. Young J, Hauptman P, Naftel D, et al. Determinants of early graft failure following cardiac transplantation, a 10 year multiinstitutional, multivariable analysis. (Presented at ISHLT meeting, April 2001, Vancouver, British Columbia).
20. Laks H, Scholl F, Drinkwater D, et al. The alternate recipient list for heart transplantation: Does it work? *J Heart Lung Transplant*. 1997;16:735-742.
21. Marelli D, Laks H, Bresson S, et al. Results after transplantation using donor hearts with preexisting coronary artery disease. *J Thorac Cardiovasc Surg*. 2003;126:821-825.
22. Kirklin JK, Young JB, McGiffin DC. *Heart Transplantation*. Philadelphia: Churchill-Livingstone, Philadelphia; 2002.
23. Freimark D, Aleksic I, Trento A, et al. Hearts from donors with chronic alcohol use. A possible risk factor for death after heart transplantation. *J Heart Lung Transplant*. 1996;15:150-159.
24. Khaghani A, Birks E, Anyanwu A, et al. Heart transplantation from live donors: "Domino Procedure". *J Heart Lung Transplant*. 2004;23:S257-S259.
25. DeMeester J, Smits J, Rutgerink E, et al. Iso-risk curves as a tool for clinical decision-making: Donor factors and medical urgency in cardiac transplantation. *J Heart Lung Transplant*. 2001;20:1099-1105.
26. Fuhrman G, Fuhrman F. Oxygen consumption of animals and tissues as a function of temperature. *J Gen Physiol*. 1959;42:715-722.
27. Piper H, Garcia-Dorado D. Prime causes of rapid cardiomyocyte death during reperfusion. *Ann Thorac Surg*. 1999;68:1913-1919.
28. McCrystal G, Pepe S, Esmore D, et al. The challenge of improving donor heart preservation. *Heart Lung Circ*. 2004;13:74-83.
29. Lower R, Shumway N. Studies of the orthotopic homotransplantation of the canine heart. *Surg Forum*. 1960;11:18-19.
30. Blanche C, Valenza M, Czer L, et al. Orthotopic heart transplantation with bicaval and pulmonary venous anastomoses. *Ann Thorac Surg*. 1994;58:1505-1509.
31. Freimark D, Silverman J, Aleksic I, et al. Atrial emptying with orthotopic heart transplantation using bicaval and pulmonary venous anastomoses. A magnetic resonance imaging study. *J Am Coll Cardiol*. 1995;25:932-936.
32. Sarsam M, Campbell C, Yonan N, et al. An alternative surgical technique in orthotopic cardiac transplantation. *J Card Surg*. 1993;8:344-349.
33. Jeevanandam V, Russell H, Mather P, et al. Donor tricuspid annuloplasty during orthotopic heart transplantation: long-term results of a prospective controlled study. *Ann Thorac Surg*. 2006; 82:2089-2095.
34. Banner NR, Polak JM, Yacoub M. *Lung Transplantation*. Cambridge: Cambridge University Press; 2003; p. 208.
35. Keogh A, Macdonald P, Harvison A, et al. Initial steroid-free versus steroid-based maintenance therapy and steroid withdrawal after heart transplantation. Two views of the steroid question. *J Heart Lung Transplant*. 1992;11:421-427.

36. Price G, Olsen S, Taylor D, et al. Corticosteroid-free maintenance immunosuppression after heart transplantation. Feasibility and beneficial effect. *J Heart Lung Transplant*. 1992;11:403-414.
37. Yacoub M, Alivizatos P, Khaghani A, et al. The use of cyclosporine, azathioprine, and antithymocyte globulin with or without low-dose steroids for immunosuppression of cardiac transplant patients. *Transplant Proc*. 1985;17:221-222.
38. Miller L, Wolford T, McBride L, et al. Successful withdrawal of corticosteroids in heart transplantation. *J Heart Lung Transplant*. 1992;11:431-434.
39. Pritzker M, Lake K, Reutzel T. Steroid-free maintenance immunotherapy. Minneapolis heart institute experience. *J Heart Lung Transplant*. 1992;11: 415-420.
40. Kobashigawa J, Miller L, Renlund D, et al. A randomized active controlled trial of mycophenolate mofetil in heart transplant recipients. *Transplantation*. 1998;66:507-515.
41. Higgins R, Kirklin J, Brown R, et al. To induce or not to induce: Do patients at greatest risk for fatal rejection benefit from cytolytic induction therapy? *J Heart Lung Transplant*. 2005;24:392-400.
42. Vincenti F, Kirkman R, Light S, et al. Interleukin-2 receptor blockade with daclizumab to prevent acute rejection in renal transplantation. *N Engl J Med*. 1998;338:161-165.
43. Beniaminovitz A, Itescu S, Lietz K, et al. Prevention of rejection in cardiac transplantation by blockade of the interleukin-2 receptor with a monoclonal antibody. *N Engl J Med*. 2000;342:613-619.
44. Radovancevic B, Vrtovec B. Sirolimus therapy in cardiac transplantation. *Transplant Proc*. 2003;35:171S-176S.
45. Mancini D, Pinney S, Burkhoff D, et al. Use of rapamycin slows progression of cardiac transplantation vasculopathy. *Circulation*. 2003;108:48-53.
46. Kubo SH, et al. Risk factors for late recurrent rejection after heart transplantation: A multiinstitutional, multivariable analysis. *J Heart Lung Transplant*. 1995;14:409.
47. Billingham M, Cary N, Hammond M, et al. A working formulation for the standardization of nomenclature in the diagnosis of heart and lung rejection: Heart rejection study group. *J Heart Lung Transplant*. 1990;9:587-593.
48. Stewart S, Cary NRB, Goddard MJ, Billingham ME. *Atlas of Biopsy Pathology for Heart and Lung Transplantation*. New York: Oxford University Press Inc.; 2000.
49. Mills RM Jr, et al. Heart transplant rejection with hemodynamic compromise: A multi-institutional study of the role of endomyocardial cellular infiltrate. *J Heart Lung Transplant*. 1997;16:813.
50. Rubin RH. Foreword. In: Bowden RA, Ljungman P, Paya CV, eds. *Transplant Infections*. Philadelphia: Lippincott-Raven Publishers; 1998:xiii-xiv.
51. Young LS, Rubin RH. Introduction. In: Rubin R, Young L, eds. *Clinical Approach to Infection in the Compromised Host*. 3rd ed. New York: Plenum Medical Book Company; 1994:1-4.
52. van der Meer J. Defects in host defense mechanisms. In: Rubin R, Young L, eds. *Clinical Approach to Infection in the Compromised Host*. 3rd ed. New York: Plenum Medical Book Company; 1994:33-66.
53. Rubin RH. Infection in the organ transplant recipient. In: Rubin R, Young L, eds. *Clinical Approach to Infection in the Compromised Host*. 3rd ed. New York: Plenum Medical Book Company; 1994.
54. Smart F, Naftel D, Costanzo M, et al. Risk factors for early, cumulative, and fatal infections after heart transplantation: A multiinstitutional study. *J Heart Lung Transplant*. 1996;15:329-341.
55. Miller L, Naftel D, Bourge R, et al. Infection after heart transplantation: A multiinstitutional study. *J Heart Lung Transplant*. 1994;13:381-393.
56. Sharples L, Jackson C, Parameshwar J, et al. Diagnostic accuracy of coronary angiography and risk factors for post-heart transplant cardiac allograft vasculopathy. *Transplantation*. 2003;76:679-682.
57. Fateh-Moghadam S, Bocksch W, Wessely R, et al. Cytomegalovirus infection status predicts progression of heart-transplant vasculopathy. *Transplantation*. 2003;76:1470-1474.
58. Biadi O, Potena L, Holweg C, et al. Seropositivity for cytomegalovirus predisposes to allograft vasculopathy in heart transplant recipients regardless of ganciclovir prophylaxis. *Am J Transplant*. 2004;4(8):549.
59. Potena L, Holweg C, Luikart H, et al. Asymptomatic cytomegalovirus activation leads to acute rejection in heart transplant recipients despite antiviral prophylaxis. *Am J Transplant*. 2004;4(8):453.
60. Luckraz H, Charman S, Wreghitt T, et al. Does cytomegalovirus status influence acute and chronic rejection in heart transplantation during the ganciclovir prophylaxis era? *J Heart Lung Transplant*. 2003;22:1023-1027.
61. Kirklin J, Naftel D, Levine T, et al. Cytomegalovirus after heart transplantation. Risk factor for infection and death: A multiinstitutional study. *J Heart Lung Transplant*. 1994;13:394-404.
62. Baliga R, Kadambi P, Javaid B, et al. A nationwide survey of cytomegalovirus prophylaxis and treatment in the transplant community. *Am J Transplant*. 2004;4(8):495.
63. Levitsky J, Freifeld A, Bargenquast K, et al. The clinical value of quantitative polymerase chain reaction

DropBooks

in cytomegalovirus infection after solid organ transplantation. *Am J Transplant*. 2004;4(8):339.
64. Costanzo M, Naftel D, Pritzker M, et al. Heart transplant coronary artery disease detected by coronary angiography: A multiinstitutional study of preoperative donor and recipient risk factors. *J Heart Lung Transplant*. 1998;17:744-753.
65. Penn I. Malignant neoplasia in the immunocompromised patient. In: Cooper DKC, Miller LW, Pattersen GA eds. *The Transplantation and Replacement of Thoracic Organs*. Hingham: Kluwer Academic; 1996:111-117.
66. Penn I. Neoplastic complications of organ transplantation. In: Ginns LC, Cosimi AB, Morris PJ eds. *Transplantation*. Malden: Blackwell Science Inc.; 1999:770-786.
67. DeSalvo T, Naftel D, Kasper E, et al. The differing hazard of lymphoma vs. other malignancies in the current era—a multiinstitutional study. *J Heart Lung Transplant*. 1998;17:70.
68. Costanzo M, Eisen H, Brown RN, et al. Are there specific risk factors for fatal allograft vasculopathy? An analysis of over 7,000 cardiac transplant patients. *J Heart Lung Transplant*. 2001;20:152.

6
OPCAB Treatment for Heart Failure

Mercedes Dullum and Jai Raman

Coronary artery disease (CAD) is the underlying cause of heart failure in the majority of patients. In fact it is responsible for up to two-third of the cases.[1] Myocardial infarctions (MIs) are responsible for 750,000 deaths annually. Approximately 60,000 of the survivors develop severe congestive heart failure and several more patients are left with compromised ventricular function.[2] With this increasing incidence of heart failure, the surgical management and treatment options have advanced and continue to evolve. Heart failure continues to be on the rise and carries a grave prognosis with a 1-year mortality of 50% of the patients with advanced disease. Figure 6.1 shows the standard surgical configuration of grafts in coronary artery surgery.

DropBooks

6.1. The Role of High-Risk CABG in Patients with Heart Failure

Transplantation has traditionally been the definitive therapy for advanced heart failure. Because of the growing demand and the limited donor supply, there has been an increase in the nontransplant surgical options used to treat heart failure. These include high-risk coronary artery bypass grafting (CABG), valve surgery, and other techniques focusing on treating the ventricular remodeling process such as ventricular restoration or reconstruction.[3] In a study evaluating the outcomes of outpatients referred to a tertiary heart center for transplantation, it was found that less than one-fifth of them ultimately had transplants. The median term survival of patients treated with alternative surgical strategies was equivalent to that of those who underwent cardiac transplantation. Of the group of patients on nontransplant surgery, 11% had high-risk CABG only and 10% had high-risk CABG with valves.

To achieve the best outcomes in this high-risk group it is important to assess the underlying etiology of the heart failure and to treat the initiating problem as well as the end result. Coronary revascularization has emerged as a successful therapy for these high-risk patients. Earlier use of appropriate inotropic support and innovative adjunctive techniques provide stability postoperatively and have allowed us to obtain these encouraging results. These include liberal use of the intra-aortic balloon pump (IABP) preoperative as well as pharmacologic therapy, particularly phosphodiesterase inhibitors such as milrinone which allows for biventricular contractility and reduces right-sided circulatory failure. These high-risk patients have a significant incidence of vasoplegia or a vasodilatory state and unlike patients with cardiogenic shock who have appropriately increased vasopressin levels, these patients have sub-physiologic levels of this hormone in circulation. Many of these patients need to have early intervention to improve their hemodynamics by initiating balloon pump support and, if necessary, the very early institution of ventricular assist devices to support end-organ perfusion while allowing the ischemic myocardium the required 2–3 days to regenerate depleted adenosine triphostate (ATP) stores. Although ischemic heart disease is the most common cause of heart failure, optimal treatment

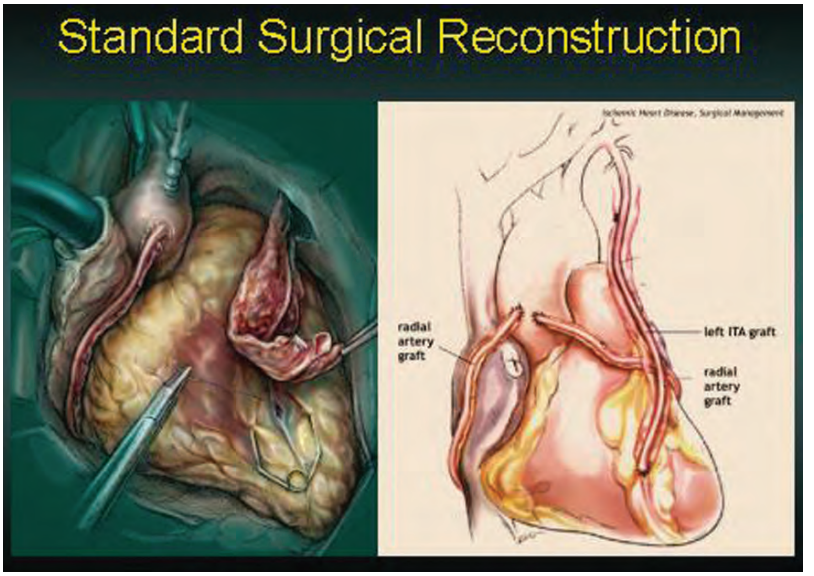


FIGURE 6.1. A left internal mammary artery being anastomosed to the LAD in the left panel; the completed set of grafts that follows is shown in the right panel.

sometimes still is unclear. Medical management is limited in effectiveness and results in high mortality and morbidity. Revascularization should be the procedure of choice in this high-risk group of patients with IHD in the presence of impaired left ventricular function. Patients are frequently referred for revascularization. However, comorbid conditions that influence the surgical mortality have been most important in the evaluation of these patients. These factors include status of the patient, acuteness of presentation, right ventricular failure, and presence of good surgical targets.[4] The surgical mortality has decreased to less than 5% in these patients. In order to assess whether these heart failure patients will benefit from surgical revascularization, it is important to differentiate between hibernating myocardium and scarred nonfunctional muscle. In patients with ischemic hibernating myocardium, coronary revascularization will result in improved function. However, when the majority of the myocardium is necrotic, scarred, and nonfunctional, this will result in higher mortality. Assessment of these patients is difficult as many of them have a mixed pattern of scar and viable tissue. There are several techniques available to assess myocardial ability, including dobutamine stress echocardiography, Thallium-201 scintigraphy, and positron emission tomography (PET). These methods are used to assess different mechanisms in myocyte viability-preserved uptake of exogenous glucose for PET, sarcolemmal integrity for Thallium -201, and the presence of inotropic contractile reserve for dubotamine echocardiography. In patients with normal or moderately impaired left ventricular function, their positive predictive value is equivalent. Dobutamine stress echocardiography appears to carry a higher false-negative rate than Thallium-201 and PET in patients with severe ventricular dysfunction and heart failure. Although a positive dobutamine stress echocardiography provides good evidence of viability, definite investigation must be done before a patient with a negative test is considered unlikely to benefit from revascularization.[5] There is a consistent relationship between the amount of viable myocardium and the improvement in the left ventricular function following revascularization.[6] A number of small studies have indicated that in order to obtain a significant improvement in left ventricular function greater than 50% of the ventricular myocardium needs to show convincing evidence of viability.[7] The risk of myocardial damage at the time of CABG must be weighed against the benefit of revascularizing hibernating

myocardium when deciding to operate on patients with heart failure. Low ejection fraction and low functional classes independently increase the risk of bad outcome. Severe left ventricular dysfunction is usually defined as left ventricular ejection fraction (LVEF) less than 35%. A series of CABG in patients with poor ventricular dysfunction demonstrated high mortality of 11–16%. However, in more highly selected patients, lower mortality rates (2.1%–6.6%) have been obtained and are secondary to the advances to patient selection, particularly establishing hibernating myocardium and improvements in myocardial preservation during surgery and anesthetic techniques. The benefits of revascularization in patients with severe heart failure have been substantial improvement in left ventricular function, tolerance, and quality of life. Another significant benefit of revascularizing the myocardium is to arrest the remodeling process in the nonischemic myocardial region, thereby reducing subendocardial ischemia, subsequent hypertrophy, and preventing further dilation. It is known that left ventricular end-systolic volume is an important prognostic for congestive heart failure and death after MI and coronary bypass. Left ventricular remodeling is defined as enlargement and distortion where segments of viable muscles undergo changes and dilate remote from the scar. This occurs in at least 30–40% of patients after a transmural infarction. This normokinetic myocardial remodeling begins as early as 4 weeks after infarction with shrinkage and subsequent changes to the area around the scar for up to 3 years later.

6.2. Choice of Technique of Surgical Revascularization (OPCAB Versus Conventional CABG)

Many efforts have been used to decrease the risk of the surgery and the associated postoperative morbidity and mortality. Even though these high-risk patients can be successfully revascularized with conventional cardiopulmonary bypass techniques, with CABG, there has been an interest in revascularizing these high-risk patients off pump (off-pump coronary artery bypass, OPCAB) in an effort to limit the myocardial injury associated with aortic cross-clamping, ensuing global myocardial ischemia, and cardioplegia-related dysfunction. Off-pump surgery also aims to eliminate the ischemic inflammatory response elicited by cardio pulmonary bypass (CPB).[8]

Even though these high-risk heart failure patients can be successfully revascularized with conventional coronary artery bypass (CCAB) techniques, there has been interest in performing this surgery off pump or without the aid of cardiopulmonary bypass. This is primarily because techniques of myocardial protection and hemodynamic management have improved.

In evaluating patients who would benefit from avoiding the “pump” or extracorporeal circulation, the primary indications are often

- Older age
- Patients with diseased ascending aortas and aortic arches
- Renal dysfunction
- Patients with significant myocardial dysfunction
- Patients with poor respiratory function
- Patients with severe liver dysfunction that may preclude anticoagulation required for CPB

These groups include patients with severe preoperative comorbidities and patients with advanced left ventricular function who poorly tolerate superimposed bypass and inflammatory injured tissues.[9] An early report comparing myocardial revascularization on and off pump in patients with ejection fraction less than 35%, there was a higher prevalence of lower ejection fraction less than 20% in the OPCAB group. The average number of grafts was similar with the similar number of the internal thoracic or mammary arteries being used. There seemed to be a trend toward lower operative risk in the off-pump group and better long-term survival in these off-pump patients versus the on-pump patients.[10]

Figure 6.2 shows a completed set of grafts in a typical off-pump procedure, with two pedicled IMA grafts and an aortocoronary graft with the radial artery grafted to the intermediate coronary artery.

It has also been shown in a large database that CABG reduced the likelihood of additional readmissions in the ensuing year over the medical management or percutaneous intervention.[11] A comparison of OPCAB patients with

DropBooks

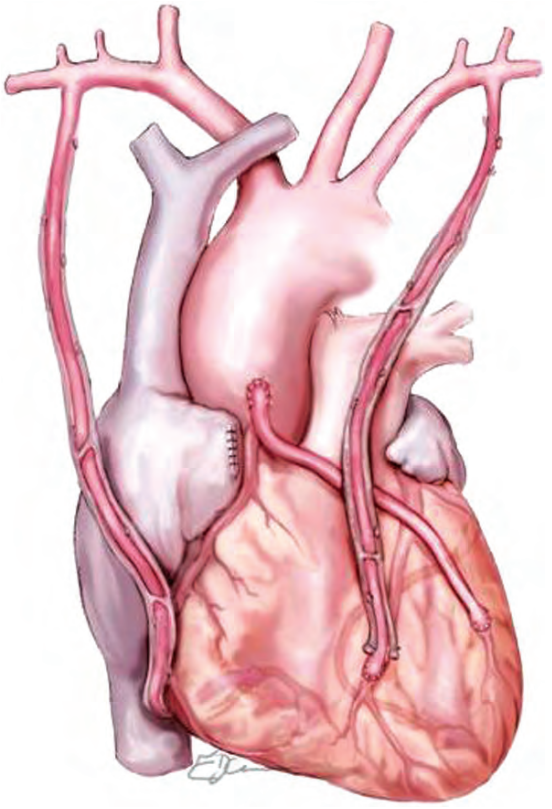


FIGURE 6.2. Two pedicled internal mammary artery grafts with an aortocoronary graft to an intermediate coronary artery.

low ejection fraction showed similar results to patients with a normal ejection fraction undergoing conventional on-pump CABG. In spite of the unfavorable risk factors, off-pump coronary artery surgery in patients with ventricular dysfunction, left main coronary artery stenoses, etc. could be safely performed with a mortality of 2.5%.[12] The hospital length of stay was also similar in both groups. Another large series looked at 1,075 patients undergoing OPCAB between October 1996 and June 2001, looking at high-risk patients which included patients with poor left ventricular function, ejection fraction less than 30%, advanced age greater than 70 years, left main coronary artery stenosis, acute myocardial function, and redo coronary artery surgery. Comparing these patients with over 2,000 patients with similar characteristics who underwent CABG on cardiopulmonary bypass, the results showed that the average number of grafts was comparable (3.0 in the OPCAB group and 3.2 in the on-pump group; the hospital mortality was 3.2% for the OPCAB group and 4.5% for the conventional CABG group). The ICU stay and hospital stay were significantly lower in the off-pump group and showed that these patients could be safely revascularized without CPB.[13] Patients with significant systolic dysfunction (preoperative ejection fraction less than 40%) undergoing off-pump surgery showed significant improvement postoperatively in this series. A more recent study published by Dr Calafiore evaluated the 30-day and late results in high-risk patients with a Euroscore greater than or equal to 6 undergoing CABG. Isolated myocardial revascularization with and without cardiac pulmonary bypass was compared with propensity score matching. This showed that in a propensity-matched group of 510 OPCAB with 510 conventional CABG, the OPCAB group had better early outcomes and similar clinical results.[14] The 30-day mortality was higher in the conventional CABG group, 5.9% versus 3.1%. There was also a significantly lower evidence of cerebrovascular accidents (CVAs). A stepwise, multivariate logistic regression analysis confirmed that CPB was an independent predictor for a higher early mortality (odds ratio of 2.0), as were CVA, and early major recurrence of chest pain. Five-year freedom rates from the events (death due to any cause, death, AMI, infarction in a grafted area, redo intervention, and any event) were similar in both groups.

Figure 6.3 shows an off-pump coronary artery bypass graft being constructed, with the left anterior descending artery (LAD) immobilized by the Octopus suction stabilizer.

6.3. Key Deciders for OPCAB or OnCAB

It seems clear that revascularization is indicated in the management of heart failure and CAD. Particularly in this high-risk group of patients, OPCAB seems the preferable approach. In the presence of greater that 2+ mitral regurgitation, patients should have the mitral valve repaired in heart failure. Arom and colleagues studied in a retrospective fashion 45 OPCAB versus 102 conventional

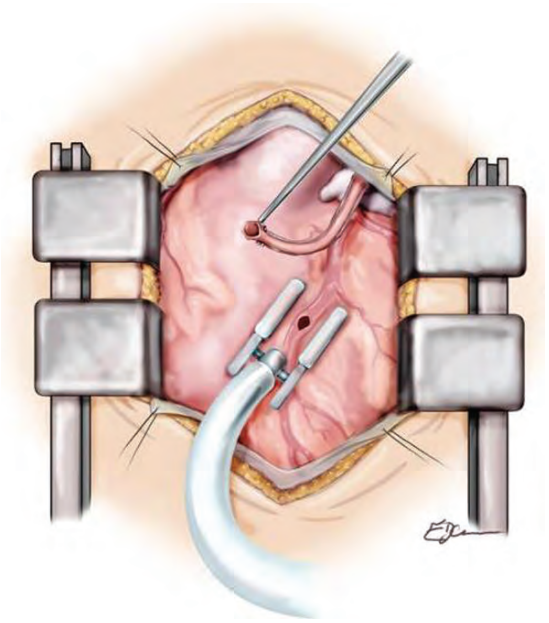


FIGURE 6.3. The LAD being stabilized by a suction-based stabilizing device to facilitate the LIMA to LAD anastomosis.

CABG recipients with ejection fractions less than 30%.[15] It was shown that cardiac displacement was well-tolerated in these patients. Fewer grafts were performed in the OPCAB group. However, the incidence of adverse events was comparable for all variables studied. Meharwal and colleagues published a large study with 355 patients with ejection fractions of 30% or less with an average age of 58 years. The number of grafts in this group was 2.8, compared with 3.3 for the on-pump cohort and mortality was 3.9%. The incidence of atrial fibrillation, length of ventilation, and hospital stay was reduced in the off-pump patients. This group of patients from India appeared to be younger and with less severe disease than reported in most CABG series in the recent literature.

Complete revascularization is very important in achieving good results in patients with severe left ventricular systolic dysfunction.[16] Completeness of revascularization has been shown to improve early survival in young and elderly patients, and is a critical factor in patients with left ventricular dysfunction. The liberal use of balloon pump support, appropriate inotropic support, hemodynamic monitoring, and perioperative analgesia are all important in an ensemble approach. This is even more necessary for exposure of lateral wall targets (branches of the circumflex artery) to achieve complete revascularization. The importance of preoperative optimization allows for a successful coronary revascularization in patients with heart failure and has been shown by Deitl et al. to improve survival in this cohort of patients with EF less than 25%.[17]

Figure 6.4 is an operative photograph showing an apical positioning device and a stabilizer (both suction based) used to expose the circumflex artery along the lateral wall of the left ventricle.

In patients with ejection fraction of lower than 25%, one predictive factor of better outcome was preoperative balloon pump insertion as compared to those who did not receive counterpulsation support. An important concept for coronary revascularization, when OPCAB is considered, is vigilant and responsive anesthesia along with good communication between anesthetic and surgical teams. It is essential for the surgeons to inform the anesthesiologists about the number of grafts required, the sequence of grafting, the nature of the occlusion of the target vessel, etc. On the part of the anesthesiologists, constant hemodynamic monitoring of blood pressure, filling pressures, and ventricular wall motion with transesophageal echocardiography (TEE) is very important for successful outcomes. It is vital to have a dedicated anesthesiologist with vigilant surveillance and management of the hemodynamics to allow the

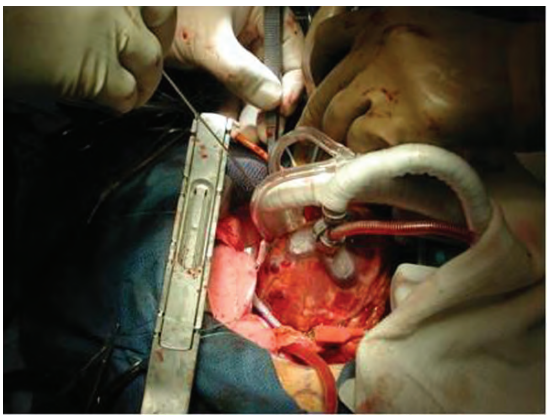


FIGURE 6.4. An apical positioning device along with the suction device to facilitate exposure to the arteries of the lateral wall; note vein graft to the circumflex.

DropBooks

performance of the procedure in an expeditious and safe fashion.

6.4. Contraindications to OPCAB

There are certain instances when off-pump surgery may not be possible. These can be in patients with very stiff myopathic hearts that do not tolerate manipulation, in which case two options are possible:

– Leave lateral wall revascularization to percutaneous intervention or use pump-assisted CABG but with the heart beating.
– Indeed, in patients who have profound ventricular dysfunction with hemodynamic alterations, the best option may be a PCAB or Pump-Assisted CABG.

Discounting the inflammatory cascade from use of cardiopulmonary bypass, this may be the safest approach in sick patients with very low ejection fractions and profound left ventricular dysfunction. Often, the circulation is supported by intra-aortic balloon counterpulsation, which provides pulsatile flow. Our own experience with this technique has been very satisfactory. It also allows the addition of other procedures, such as left ventricular reconstruction, mitral valve repair, etc., in patients who require these procedures.

The other philosophical point is the choice of conduit. It is virtually standard to use the left internal mammary artery (LIMA) to graft the LAD, because of excellent long-term patency. This finding spawned the idea that two arteries are better than one and three better than two. This mode of practice tends to ensure a lower prevalence of heart failure in patients who have previously received multiple arterial grafts.[18] Despite this, the standard coronary artery bypass procedure in the USA utilizes a LIMA and saphenous vein from the thigh. Coronary artery surgery in emerging markets such as India and China shows a great deal more sophistication, with over 60% of patients in India receiving at least two arterial grafts.

Figure 6.5 shows all arterial grafts performed without any aortic manipulation, which truly provides the full benefits of off-pump surgery. Note that one limb of radial artery has been used to prolong the right internal mammary artery (RIMA), providing a composite graft that can revascularize the inferior wall. The other segment of radial artery is anastomosed to the mid-portion of the LIMA, end-to-side to allow grafting of the lateral wall.

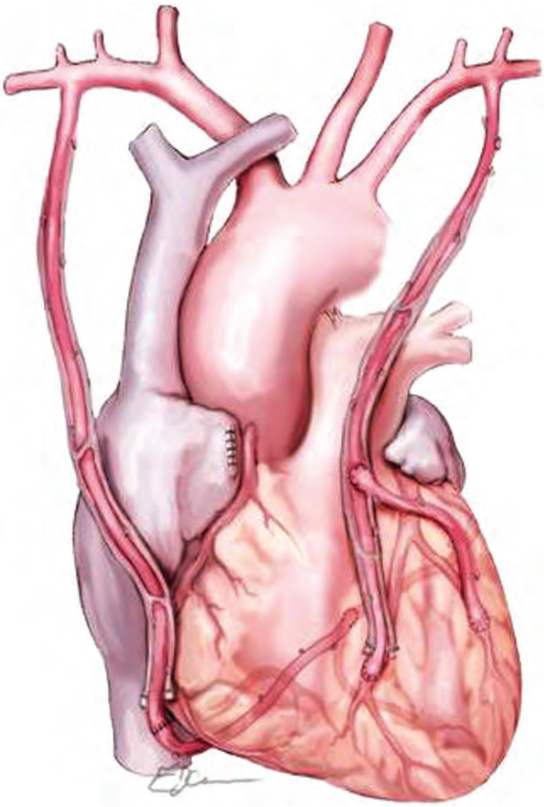


FIGURE 6.5. All arterial grafting with no aortic manipulation. Two pedicled IMA grafts with one radial artery segment extending the RIMA and the other radial artery segment hooked up to LIMA as inflow.

6.5. Operative Techniques

Successful operative technique performance of off-pump surgery requires a coordinated team approach with an experienced anesthesiologist and a cardiac surgeon comfortable with performing off-pump surgery.

In these high-risk patients, a Swan Ganz catheter and TEE are important in maintaining normal hemodynamic performance. Also in patients with left ventricular dysfunction, the preoperative optimization of cardiac performance is essential. This

may require preoperative or IABP placement and the use of cardioactive drugs, in particular, phosphodiesterase inhibitors. A thorough TEE should be used to assess left ventricular wall motion, presence and degree of valvular regurgitation, severity of atheroma of the aorta, and right ventricular function. Presence of more than 2+ mitral insufficiency is a contraindication to off-pump revascularization. In view of the emerging data supporting mitral repair in the presence of ischemic cardiomyopathy, repair of the mitral valve should be considered in any one with 2+ or greater regurgitation. Preoperative planning is also very important in successful off-pump surgery. It is necessary for the surgical team to know the vessels that will be grafted, study the anatomy and the coronary vessels involved. There should be a clear plan for the kind of conduit to be used and vessels to be revascularized. Cardiac manipulation and displacement should be performed very carefully without hemodynamic perturbation in a measured fashion to prevent rapid swings and changes in blood pressure. This requires cooperation and active participation of the anesthesiologist who would know what to do and not overreact. Continual communication between the surgeon and the anesthesiologist is also important to ensure smooth conduct of the operation. In patients with left main or tight LAD lesions or ones with severe heart failure, one easy technique of positioning by gently putting a glove behind the heart and filling it with warm saline, which gently positions the LAD into the center of the incision, is effective. This allows easy access for grafting. Grafting the LAD first establishing flow through the septal perforators and the septum allows the patient to be stable and tolerate further manipulation. The use of positioning and stabilizing devices has made a huge difference in the ability of surgeons to operate on vessels on the lateral and inferior wall.

Surgical philosophy when deciding on off-pump surgery:

1. Decide if the procedure is being performed off-pump or not, and inform the anesthesiologists and nurses.
2. If OPCAB is the technique of choice, try lifting the heart to visualize the back and/or insert deep pericardial stay sutures. These allow the surgeon to get a feel for whether the patient will tolerate off-pump surgery. If not, convert to on-pump surgery.
3. Decide on the conduits to be harvested and ensure the LIMA is harvested first for the LAD graft.
4. Decide on sequence of grafting, preferably constructing the LIMA to LAD first.
5. Thereafter, proceed with a sequence to effect revascularization to the next most ischemic area. If another pedicle graft is used, such as the RIMA, perform this next. If aortocoronary grafts are planned, try to perform the aortic anastomosis first so that when the distal anastomoses are completed, there is instant revascularization of that territory.
6. If there are issues with rhythm, use atrial pacing or dual chamber pacing with ventricular pacing wires placed on both ventricles.

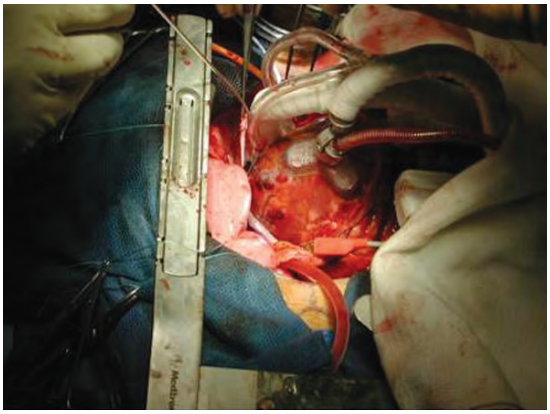


FIGURE 6.6. Facilitating grafting in difficult situations. Positioning the heart to allow the stabilizer to be used, along with the pacing. Note the pacing cable at the bottom of the picture.

Figure 6.6 shows an operative photograph with pacing cables used to speed up the heart rate.

6.5.1. Stabilization of the Heart

One of the most important advances in the evolution of off-pump surgery was the development of stabilizers. These are suction-based, traction-based or, pressure-based devices that stabilize portions of the heart where the arteries course on the surface, allowing for some reduction in the constant movement of the heart. The most successful of these is

DropBooks

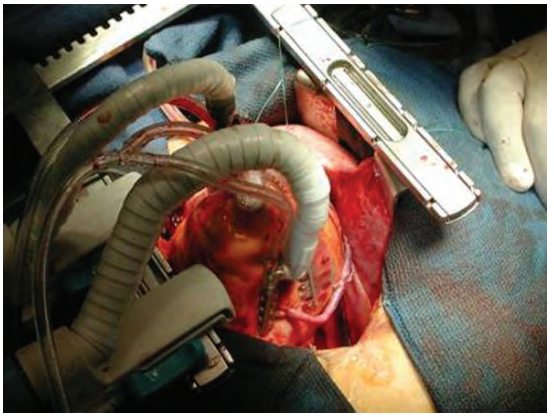


FIGURE 6.7. Heart positioned with stabilizer and positioner, with a completed distal anastomosis to an artery on the inferolateral wall.

the Medtronic Octopus, which is suction based and was initially developed by research workers at the University of Utrecht, Netherlands. Various positioning devices were then also developed to help move the heart around. Most off-pump procedures require a combination of a positioner and a stabilizer for each of the distal coronary anastomoses.

Figure 6.7 shows the suction-based apical positioning device and the stabilizer, allowing access to the inferolateral wall of the LV.

6.5.2. Special Tips in OPCAB Surgery

In general the sequence of the operation follows a philosophy, as mentioned. The goal should be for complete revascularization. In some instances, positioning of the heart can be performed by opening of the pleura and allowing the right heart to flop over into the right chest. This allows easy access to the circumflex vessels with minimal hemodynamic disturbance. However, this can be of concern if the LIMA or LITA has been grafted to the LAD as there may not be enough length to allow distraction to the heart and this needs to be considered in planning the sequence of grafting. To complete the revascularization, the other distal vessels of the lateral wall and the inferior wall can then be grafted. The proximal anastamoses can be performed to the aorta with a single partial clamp or by use of the proximal anastomotic devices, such as the U-clip Spider (clampless anastamotic devices) or the Heart String (which is a clampless way of providing a safe aortotomy).

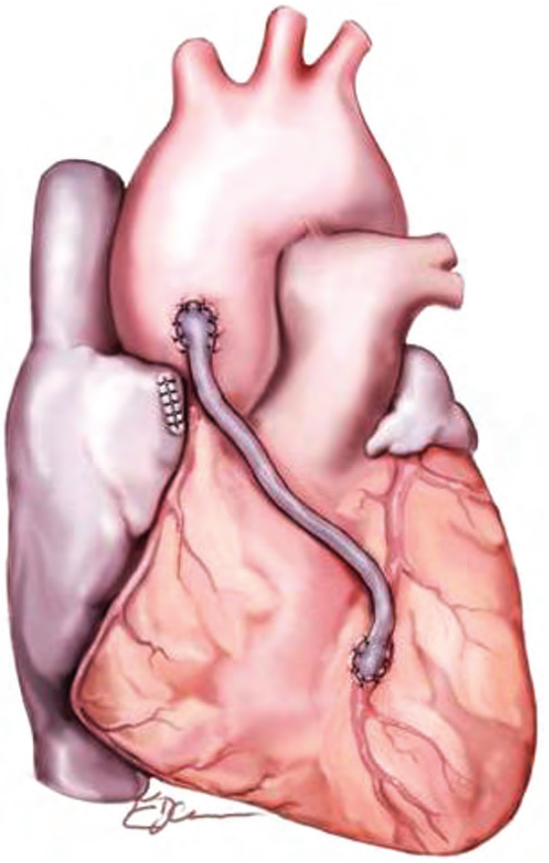


FIGURE 6.8. A saphenous vein graft to the LAD, performed with interrupted U-clips—using technology to bolster an obsolete approach.

Figure 6.8 shows a single aortocoronary graft performed to the LAD using a saphenous vein with interrupted U-clips. This can be a particularly useful strategy in redo surgery, where the proximal anastomosis can be performed without a clamp.

However, most of these devices are restricted to large caliber vein (these typically are harvested from the thigh and have poor long-term patency). To allow for immediate revascularization, the proximal anastamoses can be performed first. Intracoronary shunts can also be used for these high-risk patients to allow for coronary perfusion during the anastamoses. Intraoperative graft assessment should be performed to assess the success of the revascularization. Blake drains or similar soft

drains can be used for postoperative drainage. If necessary, cardiac function can be improved by temporary pacing wires with pacing at a higher rate to facilitate improved cardiac output.

6.5.3. Minimally Invasive Coronary Artery Surgery

Figure 6.9 demonstrates the use of bilateral internal mammary arteries to graft the left side, namely the LIMA to the circumflex marginal artery and the RIMA to the LAD. This is the preferred approach for robotically assisted minimally invasive CABG. Some of these can be performed purely through small incisions made for the ports and is then known as TECAB (totally endoscopic coronary artery bypass).[19] Alternatively, these can be performed through a left mini-thoracotomy (Thora-CAB), after harvesting the LIMA and RIMA with the aid of the Da Vinci "robot." These procedures have a few ardent adherents at specialized centers that have unrestricted access to the Da Vinci robot. Long-term results of these procedures are not known.

Finally, in many studies, it has now been shown quite conclusively that the long-term outcome with conventional coronary artery surgery is significantly better than that with percutaneous techniques, such as angioplasty and stenting.[20]

Figure 6.9 shows the typical configuration of bilateral pedicled IMA grafts performed off-pump through a minimally invasive approach (either TECAB or Thora-CAB).

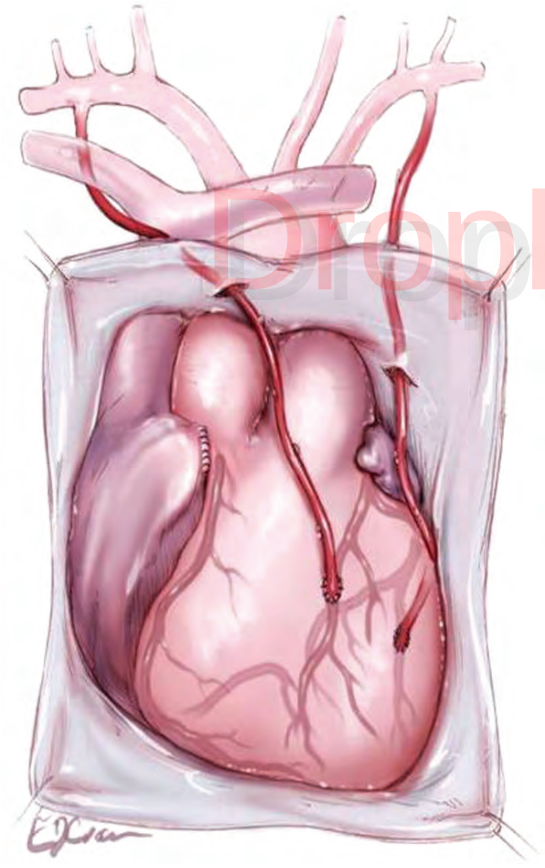


FIGURE 6.9. Bilateral pedicled skeletonized internal mammary arteries—LIMA to circumflex marginal and RIMA to LAD.

6.6. Hybrid Procedure

In a subset of patients with severe heart failure who may also have significant morbidity, such as renal comorbidities, or who may not recover from a sternotomy or partial sternotomy, a hybrid approach is a very attractive option. In view of the improving stent technology, this may become the future of revascularization. Hybrid revascularization entails surgical revascularization combined with transcatheter therapy.

Usually the LITA is grafted to the LAD in a minimally invasive fashion. This can be performed by a thoracotomy or sub-xyphoid MIDCAB approach.[21] The other less important vessels can then have a stent placed percutaneously. In general, the sequence is to perform the graft and percutaneous placement of the stent, within the same day or within 48 h. This sequence of revascularization has two benefits and in the case of left main disease, i.e.,

1. The LAD is then protected by graft, and
2. The anastomosis can be evaluated at the time of angiography.

This hybrid approach allows for a less invasive approach to complete revascularization. It can also be used in redo patients where the back or wall vessels can be grafted through a thoracotomy with inflow from the descending aorta with stenting of the other vessels.

DropBooks

OPCAB revascularization has been shown to be as effective and safe as conventional coronary bypass.[22] In the high-risk patient, particularly those with heart failure, left main disease, or severe ventricular dysfunction (LVEF) less than 35%, complete revascularization can also be performed and is also more beneficial in this high-risk population. These patients do need to be optimized and the procedure needs to be performed by an experienced team to obtain good outcomes.

6.7. Arterial Grafts to Prevent Heart Failure ?

The philosophical imperative to use more arterial grafts stems from long-term patency data comparing internal thoracic or mammary arteries with saphenous vein grafts. One of the largest real-world experiences comes from Brian Buxton's database in Melbourne which conclusively showed a dramatic divergence in patency starting at 3 years, progressing dramatically over 20 years. Interestingly, the patency of the IMA graft remains similar over those 20 years with no further decline in patency.

Figure 6.10 is a graphical representation of the cumulative patency of internal thoracic artery grafts compared to saphenous vein grafts, from the largest longitudinal database of its kind (kind courtesy of Prof Brian Buxton, University of Melbourne and Epworth Hospital Databases—maintained by Prof Buxton and Dr J Fuller).

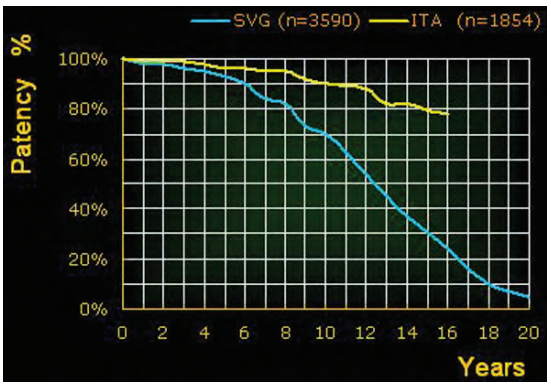


FIGURE 6.10. Cumulative patency of saphenous vein grafts compared to the internal mammary artery or internal thoracic artery—University of Melbourne database, courtesy of Prof B Buxton.

As a consequence, redo coronary artery surgery, reintervention for vein graft disease, and heart failure from failing vein grafts form a small load of the heart failure population in the areas served by the University of Melbourne surgeons. While this is observational data, this is probably due to the high use of multiple arterial grafts. The results of the RAPCO (Radial Artery Patency and Cumulative Outcomes) study set up by Buxton and Raman in 1996 are awaited in 2007–08 with great interest.

Off-pump CABG with complete revascularization has been shown to be as effective and safe as conventional coronary bypass and complete revascularization to be performed off-pump (Puskas). In the high-risk patient, particularly those with heart failure, the left main disease or severe ventricular dysfunction (LVEF less than 35%), complete revascularization can also be performed using OPCAB. This technique can be more beneficial in this high-risk population. These patients do need to be optimized and the procedure needs to be performed by an experienced team to obtain good outcomes. To successfully perform this, the surgeon needs to have many options on the approach for revascularization and with the advances in off-pump techniques, this can be readily performed. A strategy of off-pump surgery utilizing arterial grafts as in Figure 6.11 may be the innovative way of preventing heart failure (the off-pump approach reduces the early perioperative myocardial dysfunction and the arterial grafts provide better patency, thereby preventing development of heart failure).

6.8. Keypoints

Coronary artery surgery provides a very suitable primary surgical modality in the treatment of heart failure as a consequence of CAD.

Off-pump coronary artery bypass surgery may have particular advantages in high-risk patients with left ventricular dysfunction.

Appropriate choice of arterial conduits may confer protection against future episodes of heart failure.

Coronary artery surgery remains the cornerstone for a lot of surgical techniques in the treatment of heart failure.

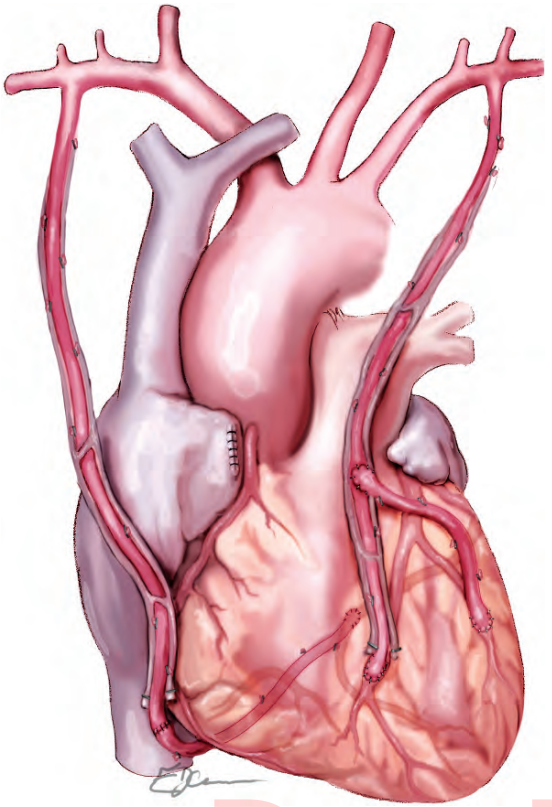


FIGURE 6.11. All arterial grafts—using both pedicled IMAs and radial arteries—this strategy combined with beating heart techniques may prevent heart failure in the short and long term. Note the radial artery extension of the RIMA and the radial artery jump graft off the LIMA.

DropBooks

References

1. ACC/AHA Guidelines. *Circulation*. 2001;104:2996.
2. Oz M. Surgical issues in heart failure: What's new? *J Card Fail*. 2001;7(2):S18-S24.
3. Mahon N, O'Neill J, Young J, et al. Contemporary outcomes of outpatients referred for cardiac transplantation evaluation to a tertiary heart failure center: Impact of surgical alternatives. *J Card Fail*. 2004;10(4):273-278.
4. Griffith B. Surgical treatment of congestive heart failure: Evolving options. *Ann Thorac Surg*. 2003;76: S2254-S2259.
5. Pagano D, Townend J, Bonser R. What is the role of revascularisation in ischaemic heart failure? *Heart*. 1999;81:8-9.
6. Pagano D, Townend J, Horton R, et al. Coronary artery bypass grafting for ischemic heart failure. The predictive value of quantitative PET for symptomatic and functional outcome. *J Thorac Cardiovasc Surg*. 1998;115:791-799.
7. vom Dahl J, Eitzman DT, al Aouar ZR, et al. Relation of regional function, perfusion, and metabolism in patients with advanced coronary artery disease undergoing surgical revascularization. *Circulation*. 1994;90:2356-2366.
8. Menasche P. The systemic factor: The comparative roles of cardiopulmonary bypass and off-pump surgery in the genesis of patient injury during and following cardiac surgery. *Ann Thorac Surg*. 2001;72: S2260-S2266.
9. Sternik L, Moshkovitz Y, Hod H, Mohr R. Comparison of myocardial revascularization without cardiopulmonary bypass to standard open heart technique in patients with left ventricular dysfunction. *Eur J Cardiothorac Surg*. 1997;11:123-128.
10. Anderson A, Smart F, Battaglia S, et al. Treatment modalities, mortality, and readmissions for congestive heart failure patients [abstract]. *JACC*. 2002;8(4). Abstract 251.
11. Jasinksi M, Stanislaw W, Olszowka P, et al. Dysfunction of left ventricle as an indication for off-pump coronary artery bypass grafting. *HSForum*. 2003;6(6):E85-E88.
12. Meharwal Z, Mishra Y, Kohli V, et al. Off pump multivessel coronary artery surgery in high-risk patients. *Ann Thorac Surg*. 2002;74:S1353-S1357.
13. Giesler G, Butkevich A, Croitoru M, et al. Off pump coronary artery bypass surgery leads to improvement of left ventricular function in patients with significant systolic dysfunction. The 8th annual scientific meeting HFSA S67.#183.
14. Calafiore A, DiMauro M, Canosa C, et al. Early and late outcome of myocardial revascularization with and without cardiopulmonary bypass in high risk patients (EuroSCORE ≥6). *Eur J Cardiothorac Surg*. 2003;23:360-367.
15. Arom KV, Flavin TF, Emery RW, Kshettry VR, Petersen RJ, Janey PA. Is low ejection fraction safe for off-pump coronary bypass operation ? *Ann Thorac Surg*. 2000;70:1021-1025.
16. Goldstein D, Beauford R, Garland P, Saunders C. Multivessel off-pump revascularization in high-risk patients. In: Oz MC, Goldstein DJ, eds. *Minimally Invasive Cardiac Surgery*. 2nd ed. Totowa, NJ: Humana Press; 2004:229-239.
17. Dietl CA, Berkheimer MD, Woods EL, Gilbert CL, Pharr WF, Benoit CH. Efficacy and cost-effectiveness of preoperative IABP in patients with ejection fraction of 0.25 or less. *Ann Thorac Surg*. 1996;62:401-408.
18. Shah PJ, Gordon I, Fuller J, et al. Factors affecting saphenous vein graft patency: Clinical and angio-

graphic study in 1402 symptomatic patients operated on between 1977 and 1999. *J Thorac Cardiovasc Surg*. 2003;126(6): 1972-1977.
19. Boyd WD, Kodera K, Stahl KD, Rayman R. Current status and future directions in computer-enhanced video- and robotic-assisted coronary bypass surgery. *Semin Thorac Cardiovasc Surg*. 2002; 14(1): 101-109.
20. Taggart DP. Thomas B Ferguson Lecture. Coronary artery bypass grafting is still the best treatment for multi-vessel coronary artery and left main disease, but patients need to know. *Ann Thorac Surg*. 2006;82(6):1966-1975.
21. Dullum MKC, Block J, Qazi A, Shawl F, Benetti F. Xyphoid MIDCAB: Report of the technique and experience with a less invasive MIDCAB procedure. *Heart Surg Forum*. 1999;2(1):77-81.
22. Puskas J, Thourani V, Marshall J, et al. Clinical outcomes, angiographic patency, and resource utilization in 200 consecutive off-pump coronary bypass patients. *Ann Thorac Surg*. 2001;71: 1477-1484.

7
Circulatory Support for Bridging to Recovery or Transplantation

Francis D. Pagani

7.1. Indications for Device Support and Patient Selection

The goal of circulatory support as a bridge to recovery or transplantation is to restore normal hemodynamics and oxygen delivery while permitting recovery of end-organ function. There are no absolute hemodynamic criteria to meet in order to initiate circulatory support; therefore, appropriate judgment and clinical experience is required to select the proper patients and intervene at an appropriate time. In the setting of acute myocardial infarction complicated by cardiogenic shock, a cardiac index of less than 2.2 L/min/m^2, systolic blood pressure of less than 90 mmHg, pulmonary capillary wedge pressure of greater than 15 mmHg, with manifestations of poor tissue perfusion reflected by oliguria, rising serum creatinine and liver transaminases, acidosis, mental status changes, and cool extremities, are associated with a mortality in excess of 50% at 30 days.[1] This high mortality occurs despite the availability of optimal pharmacologic therapy, invasive monitoring, thrombolysis, and intraaortic balloon pump (IABP) support.[1] Thus, in the appropriate clinical setting, circulatory support can be lifesaving. Hemodynamic criteria alone, however, should not be used as the only factor in assessing a patient's need for circulatory support. Other important considerations include the degree of inotropic support, clinical setting and findings, and time frame in which events, such as organ injury or recovery, are occurring.

Patient selection is, perhaps, the single most crucial factor in determining a successful outcome in patients who receive circulatory support. The patient's history and overall clinical setting are considered in the decision process to initiate circulatory support. Patients should not be considered for it if they have significant contraindications to circulatory support or to heart transplantation in situations where they are unlikely to wean from circulatory support once it has been initiated. Absolute contraindications to circulatory support include the presence of irreversible renal, hepatic, or respiratory failure, as well as neurologic dysfunction with significant irreversible cognitive deficits.

Increasing degrees of chronic organ dysfunction also present relative, but not absolute, contraindications to initiating temporary circulatory support. Chronic pulmonary disease associated with significantly impaired pulmonary reserve and systemic oxygenation can contribute to perioperative hypoxia and pulmonary vasoconstriction, resulting in right-sided circulatory failure. Patients with severe chronic pulmonary disease may have a fixed (not responsive to pulmonary artery vasodilators) elevation of the pulmonary vascular resistance. A pulmonary vascular resistance of more than 4–6 Wood units that is not reversible represents a contraindication to heart transplantation, and thus circulatory support in circumstances where weaning is unlikely.

Acute renal failure requiring dialysis is only a relative contraindication to initiating temporary circulatory support. In the setting of cardiogenic shock with acute renal failure, establishing normal hemodynamics with circulatory support may resolve the renal failure. The degree and duration of shock,

DjvuBooks

along with the patient's baseline renal function, must be considered in estimating the probability of recovery of renal function. Underlying "nonreversible" etiologies for renal insufficiency, including diabetic nephropathy or hypertensive renal disease, may significantly impact the degree of recovery. This is important in considering whether the patient will be a transplant candidate or not, in the event that native heart function does not recover while the patient is supported on a device.[2] Similarly, improvement in hepatic congestion and recovery of synthetic functions of the liver can occur with institution of circulatory support. The presence of portal hypertension or liver cirrhosis is an absolute contraindication to initiating circulatory support.

Age may represent a relative contraindication to initiating circulatory support if the patient is unlikely to wean, and is either too elderly or has additional comorbidities to qualify for heart transplantation. Advanced age adversely affects survival on temporary circulatory support, but does not affect the probability of weaning.[3–8]

Timing the initiation of temporary circulatory support is also crucial to patient outcome. In the setting of postcardiotomy shock, delay in initiating temporary circulatory support for >6 h after the initial weaning from cardiopulmonary bypass is associated with a significant decrease in survival; 44% versus 14%.[7,8] Early initiation of circulatory support, based on predictive models for device need using hemodynamic parameters and degree of intraoperative inotropic support, has demonstrated improved rates of weaning and survival to hospital discharge[9] (Table 7.1; Figure 7.1). As the severity of illness and organ dysfunction increase as a result of delay in instituting circulatory support, the need for biventricular support, rather than univentricular support alone, increases and results in decreased survival.[6,7,10,11] An episode of cardiac arrest prior to the initiation of temporary circulatory support significantly reduces survival, 47% versus 7%.[7,8]

Selection of the appropriate circulatory assist device is also critical to successful outcome and is dependent on a number of factors. These factors include the etiology of the circulatory failure, the duration of expected support, whether biventricular or univentricular support is required, whether combined cardiac and pulmonary failure is present, the size of the patient, the intended use for the device, and what are the current Food and Drug Administration (FDA) restrictions and regulations for a particular device. Consideration of all these factors help define the end point of therapy, which may include bridge to recovery or bridge to heart transplantation (Table 7.2).

Table 7.1. Insertion criteria for implantation of ventricular assist devices[a].

Hemodynamic criteria	
Systolic blood pressure	<100 mmHg
Mean pulmonary artery pressure	>25 mmHg
Central venous pressure	>15 mmHg
Cardiac index	<2.0 L/min/m^2
Pharmacologic criteria	
Epinephrine	≥0.15 μg/kg/min
Dobutamine	≥10 μg/kg/min
Dopamine	≥10 μg/kg/min
Milrinone	≥0.5 μg/kg/min

[a]Two or more high dose inotropes with low output triggers VAD consideration.
Source: Adapted from Samuels et al.[9]

7.2. Considerations in Instituting Temporary Circulatory Support

7.2.1. Valvular Heart Disease

Abnormalities of the cardiac valves have important consequences in patients being considered for circulatory support and may require repair or replacement in order to initiate successful circulatory support or achieve weaning from support. Mild to moderate aortic stenosis in the absence of insufficiency is not a contraindication to placement of a ventricular assist device (VAD). However, severe aortic stenosis should be corrected prior to placement of a temporary VAD, preferably with a bioprosthetic valve, to facilitate future weaning or optimize native heart function in the event of device failure. The presence of even mild to moderate aortic insufficiency can have a significant impact on the effectiveness of VADs where left ventricular assistance is initiated with left atrial to aortic cannulation. In these cases, aortic insufficiency will result in left ventricular distention in the presence of significant left ventricular dysfunction. Left ventricular distention adversely affects subendocardial blood flow and can ultimately prevent weaning from circulatory support. In cases where left ventricular assistance is initiated with devices that require left ventricular apical to aortic cannulation, reductions in left ventricular pressure elicited by mechanical assistance increase the pres-

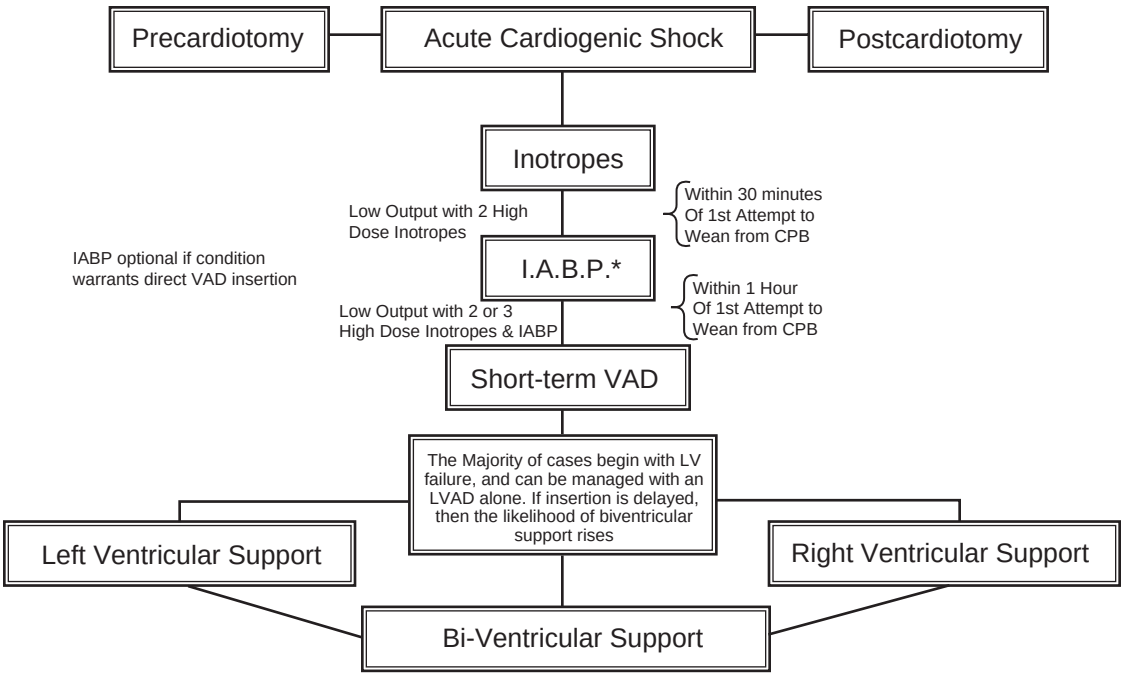

Precardiotomy
Acute Cardiogenic Shock
Postcardiotomy
Inotropes
Low Output with 2 High Dose Inotropes
Within 30 minutes Of 1st Attempt to Wean from CPB
IABP optional if condition warrants direct VAD insertion
I.A.B.P.*
Within 1 Hour Of 1st Attempt to Wean from CPB
Low Output with 2 or 3 High Dose Inotropes & IABP
Short-term VAD
The Majority of cases begin with LV failure, and can be managed with an LVAD alone. If insertion is delayed, then the likelihood of biventricular support rises
Left Ventricular Support
Right Ventricular Support
Bi-Ventricular Support

FIGURE 7.1. Algorithm for determining timing of device support. (Reproduced with permission from Samuels et al.[48] ©2007 by The Society of Thoracic Surgeons.

TABLE 7.2. List of circulatory support devices for bridge to recovery or heart transplantation.

Pump type	Intended duration of support[b]	FDA Status[a]	Indications or potential uses
Intraaortic balloon pump	Short-term	Approved	Short-term bridge to recovery
Extracorporeal rotary pumps			
ECMO	Short-term	Approved	Short-term bridge to recovery (centrifugal pumps are FDA-approved for short-term support of <6 h. Longer periods of support are considered "off-label" use).
Centrifugal pumps	Short-term	Approved	
TandemHeart pVAD	Short-term	Approved	
Impella Recovery system	Short-term	Investigative	
Extracorporeal pulsatile pumps			
Thoratec VAS	Short or long-term	Approved	Short-term bridge to recovery, bridge to transplant
Abiomed BVS 5000	Short-term	Approved	Short-term bridge to recovery
Implantable pulsatile pumps			
HeartMate XVE LVAS	Long-term	Approved	Bridge to transplant
Novacor LVAS	Long-term	Approved	
Implantable rotary pumps			
HeartMate II	Long-term	Investigative	Bridge to transplantation
DeBakey LVAD	Long-term	Investigative	
Jarvik 2000	Long-term	Investigative	
Total artificial heart			
CardioWest	Long-term	Approved	Bridge to transplantation

FDA Food and Drug Administration, *ECMO* Extracorporeal membrane oxygenation, *pVAD* percutaneous Ventricular Assist Device, *LVAS* left ventricular assist system, *LVAD* left ventricular assist device.

[a]FDA status as of June 2005.

[b]Short- and long-term designations are considered relative and generally imply days to weeks (2) for short-term duration of support and weeks to months and in some cases >1 year for long-term durations of support.

DropBooks

sure gradient across the aortic valve and increase the degree of aortic insufficiency. Thus, blood pumped into the aortic root by the device will flow backward across the incompetent aortic valve (aortic insufficiency), thereby decreasing net forward flow and compromising end-organ perfusion. Even mild to moderate aortic insufficiency may become severe with initiation of circulatory support as a consequence of reducing left ventricular end-diastolic pressure by emptying of the left ventricular cavity by the device and elevation of the aortic root pressure due to an increase in device flow. The significance of the regurgitant volume of blood can be easily determined by measuring cardiac output with a thermodilution catheter and comparing it to device flow. In cases where device flow exceeds the cardiac output by >1.5–2 L/min, the volume of regurgitation is considered significant. In addition, the presence of significant aortic insufficiency can be confirmed by echocardiography. Patients with a mechanical valve prosthesis in the aortic valve position should have the mechanical valve replaced with a bioprosthetic valve prior to institution of temporary left ventricular assistance. However, bioprosthetic valves in the aortic position are also prone to thrombosis as a result of complete unloading of the left ventricle with a VAD that obviates the need for prosthetic valve opening and closing during support. The management of aortic valve prosthesis for patients requiring long-term bridge to heart transplant or destination support with implantable devices is controversial and different strategies are necessary than for patients requiring only temporary support.[12,13]

Patients with significant preexisting mitral stenosis at the time of initiation of circulatory support may require correction of the valvular problem before initiation of circulatory support, depending on device selection and site of cannulation. In the setting of significant mitral stenosis, left ventricular filling is impaired. Device systems that utilize apical ventriculotomy for cannula placement for ventricular drainage may experience limitations in device filling due to the mitral stenosis. This problem can be circumvented by either choosing a device that can utilize left atrial drainage or by correcting the underlying valvular pathology (mitral valve repair or replacement with a bioprosthetic valve). In patients with prosthetic valves in the mitral position (either mechanical or bioprosthetic), left ventricular assist should be accomplished with left ventricular apical cannulation to ensure adequate blood flow across the mitral prosthesis to prevent thromboembolism. Mitral regurgitation does not have an impact on the filling of a left ventricular assist device (LVAD); however, elevations in pulmonary pressures may persist with severe regurgitation, and remodeling of the left ventricle may be adversely effected.[14] In situations where weaning from circulatory support may be feasible, correction of the mitral pathology, either stenosis or regurgitation, is necessary in order to optimize ventricular function.

Adequate right heart function is extremely important to maintain LVAD flow in the early postoperative period in patients on univentricular support. Severe tricuspid regurgitation can significantly impair the forward flow of blood on the right side particularly in situations of high pulmonary vascular resistance. Further, severe tricuspid regurgitation contributes to elevated central venous pressure, hepatic congestion, and renal dysfunction. Severe tricuspid regurgitation may be present preoperatively in the setting of volume overload and biventricular failure or may develop following institution of LVAD support as a consequence of right ventricular dilation from leftward shift of the interventricular septum.[15–17] If severe tricuspid regurgitation is present during the initiation of LVAD support, tricuspid valve repair should be performed to improve right-sided circulatory function.

7.2.2. Coronary Artery Disease

Patients who have significant obstructive coronary artery disease or patients with postcardiotomy shock following failed coronary bypass operations may continue to experience angina during circulatory support. The presence of obstructive coronary disease with ongoing ischemia may limit the degree of myocardial recovery, significantly impact the ability to wean from device support, or impact the ability to wean from cardiopulmonary bypass with left-sided support only in the presence of ischemia of the right ventricle. Perioperative ischemia of the right ventricle may be of hemodynamic significance during institution of circulatory support. Right ventricular ischemia causing myocardial stunning or infarction that occurs during or soon after initiation of circulatory support can

elicit right-sided circulatory failure, resulting in decreased flow to the LVAD. In patients who have had coronary bypass surgery and are candidates for circulatory support, patent bypass grafts, particularly to the right coronary artery or left anterior descending coronary artery, should be preserved in order to reduce the risk of perioperative right-sided circulatory failure and arrhythmias. In selected situations it may be important to perform a coronary artery bypass to the right coronary artery or left anterior descending coronary artery systems to optimize right heart function in the perioperative period if significant obstructive coronary lesions amenable to bypass are present in the distribution of the these arteries.

7.2.3. Arrhythmias

Atrial and ventricular arrhythmias are common in patients with cardiogenic shock and underlying ischemic heart disease or idiopathic cardiomyopathies. These arrhythmias generally persist in the immediate postoperative period and subsequently resolve with time as the hemodynamic condition of the patient improves and inotropic therapy is weaned. In patients with ongoing ventricular arrhythmias, biventricular assistance is generally indicated to ensure adequate LVAD filling. In situations where weaning from circulatory support is feasible or planned, elimination of the ventricular arrhythmias with antiarrhythmic therapy or electrophysiological ablation is essential.

7.2.4. Intracardiac Shunts

Potential intracardiac shunts such as a patent foramen ovale or atrial septal defect should be closed at the time of initiation of left ventricular assistance to prevent right to left shunting. These anomalies should be identified prior to surgery using transesophageal echocardiogram.[18] During the initiation of left ventricular assistance, left atrial pressure is reduced compared to right atrial pressure. This gradient causes shunting of deoxygenated blood from the right atrium into the left, resulting in significant systemic hypoxemia. In cases where a patent foramen ovale or atrial septal defect has been missed, treatment includes administering pulmonary vasodilators and inotropic agents to decrease the shunt by improving right heart function and lowering right atrial pressure. If significant hypoxia persists, reoperation or percutaneous interventions to close the anomaly are required.

7.3. Adverse Events Associated with Mechanical Circulatory Support

The perioperative morbidity associated with seriously ill patients requiring temporary circulatory support is significant. Bleeding, right-sided circulatory failure, neurologic dysfunction, and progressive multisystem organ failure are the most frequent complications that occur in the early postoperative period following initiation of circulatory support.

Bleeding is a frequent complication and generally requires reoperation in the early postoperative period. Risk factors for bleeding include preoperative hepatic congestion and failure, poor preoperative nutritional status, prolonged cardiopulmonary bypass times, extensive surgical dissection, reoperative surgery, multiple cannulation sites, decreased platelet function, and induction of fibrinolysis as a result of contact with biomaterial surfaces of the cardiopulmonary bypass circuit and circulatory support device. The risk of bleeding has decreased with the use of the serine protease inhibitor, aprotinin, and administration of vitamin K prior to operation.[19,20]

Right-sided circulatory failure occurs in ~10–20% of patients supported by left ventricular assistance. This incidence is significantly higher in patients presenting with multisystem organ failure. The etiology of right-sided circulatory failure is multifactorial and includes primary pathologies within the pulmonary vascular bed and/or right ventricle. Frequently, the occurrence of right-sided circulatory failure is a consequence of both. Factors contributing to right-sided circulatory failure include impaired right ventricular function as a result of air embolism, myocardial stunning as a result of poor intraoperative myocardial protection, ischemia and infarction from coronary artery disease, arrhythmias, volume loading, and alteration of right ventricular septal geometry induced by left ventricular unloading. Several studies have demonstrated that factors such as elevated central venous pressure, transpulmonary gradient greater than 16 mmHg,

DMOBooks

low preoperative right ventricular stroke work index, degree of preoperative pulmonary edema, increased need for perioperative transfusions, all increase the need for right ventricular mechanical support following left ventricular assistance.[11,21–23] Acute unloading of the left ventricle by circulatory support may cause the septum to shift leftward, increasing right ventricular volume loading and reducing its function.[15,16] The negative consequences of this phenomenon may be offset by the reduction in pulmonary artery pressures and right ventricular afterload caused by device-mediated left ventricular decompression.[15,16] Limiting device flows in the early perioperative period may prevent septal shift and right ventricular overload, and thus prevent right-sided circulatory failure in some patients. More recently, the improved perioperative management of elevated pulmonary vascular resistance including the use of inhaled nitric oxide, a specific, potent pulmonary vasodilator, in combination with milrinone, isoproterenol, or dobutamine, has significantly reduced the need for placement of a right VAD.[24]

The occurrence of thromboembolic events following circulatory support is variable and depends on a number of factors including the type of device, duration of support, location and number of cannulation sites, and the presence of prosthetic valves within the heart. Overall, ~10–30% of patients receiving circulatory support will experience a thromboembolic event. Improvement in the rate of thromboembolic events has come from more aggressive antiplatelet therapy in conjunction with heparin and warfarin anticoagulation, improved device design, and more frequent use of left ventricular apical as compared to left atrial cannulation. In patients supported for short durations only, anticoagulation is usually achieved with heparin and antiplatelet therapy. Longer term support usually requires transition to warfarin and antiplatelet therapy for most, but not all, temporary extracorporeal devices.

The incidence of early nosocomial non–device- or device-related infections in patients undergoing temporary circulatory support is ~30–40% in many series and is related to the acuity of illness in this population of patients.[25,26] Patients with persistent or recurrent sepsis and those patients with device-related infections tend to have a higher mortality than do patients without these complications. Prolonged hospitalization, immobilization, endotracheal intubation, poor nutritional status, diabetes, obesity, indwelling catheters, intravascular lines, transcutaneous cannulas, and broad-spectrum antibiotic therapy all contribute to the high incidence of nosocomial infections. Device-related infections can sometimes be successfully treated with antibiotic suppression and device exchange or removal.

7.4. Considerations in Weaning Patients from Mechanical Circulatory Support

A number of factors must be considered when weaning patients from circulatory support. First and foremost is the consideration of any pathologic abnormalities of the heart, such as valvular disease or severe coronary disease, that has not been addressed and corrected. If the underlying pathology that has caused the patient to require circulatory support is not corrected, then the chances of weaning from device support will be negligible. Cardiac tamponade must also be excluded. Bleeding is a major early complication of circulatory support, and reoperation for cardiac tamponade and bleeding is frequent. Transesophageal echocardiogram may not reliably identify cardiac tamponade in the early postoperative period. Thus, a high index of suspicion and low threshold for reoperation is critical to rule out tamponade. Volume status, preload and afterload, cardiac rhythm, and degree of inotropic support should be optimized for weaning. Noncardiac causes can contribute to failure to wean from circulatory support. Pulmonary edema, elevated pulmonary vascular resistance, acute respiratory distress syndrome, and pneumonia may hinder right ventricular function. Once a patient's status has been optimized, weaning from circulatory support with the use of transesophageal echocardiogram is ideal. As device flows are reduced, transesophageal echocardiogram provides information on ventricular filling and performance and valve function. If patients can maintain satisfactory hemodynamics with reduction of pump flow, they can be considered for weaning. In the setting of biventricular support, it is important that device flows on the right side be reduced prior to turning down left-sided device flows to prevent

pulmonary edema in the event of inadequate left-sided ventricular function. As device flows are reduced, native heart function will begin to support the circulation and monitoring of the systemic arterial waveform will demonstrate native heart contractions in synchronization with the electrocardiogram. If the hemodynamics are unsatisfactory during the weaning trial, the patient will require continued support and subsequent weaning trials. In cases where weaning from temporary circulatory support is not possible, patients should be evaluated for heart transplantation or destination therapy and bridged to a mechanical device with long-term support capabilities when feasible and indicated.

7.5. Mechanical Circulatory Support Devices

7.5.1. Intraaortic Balloon Pump

The IABP was first introduced in 1962 by Moulopolous and colleagues.[27] The first clinical use of the IABP was reported by Kantrowitz in 1968 who described the use of the pump in three patients suffering from postinfarction cardiogenic shock.[28] Since that time, the IABP has become a simple, affordable, and effective device to support patients in cardiogenic shock (Figure 7.2). The IABP can be inserted percutaneously and may augment cardiac output by as much as 10–25% depending on a number of factors that include balloon size, patient size, degree of aortic compliance, cardiac rhythm, blood pressure, IABP settings and timing, as well as etiology of the cardiogenic shock. Patients with ischemic cardiomyopathy generally have the greatest increase in cardiac output, with improved cardiac contractility resulting from enhanced coronary perfusion.

The concept for the IABP is based upon the observation that the area under the arterial pressure trace (time–tension index) is an indirect estimation of the heart's oxygen consumption and by decreasing the area during systole by reducing afterload, can effectively support the failing heart. Harken and colleagues described a device that lowered the time–tension index by withdrawing blood from the arterial tree just before ventricular systole, returning it to the circulation in diastole.[29] In 1962, Moulopolous and associates described

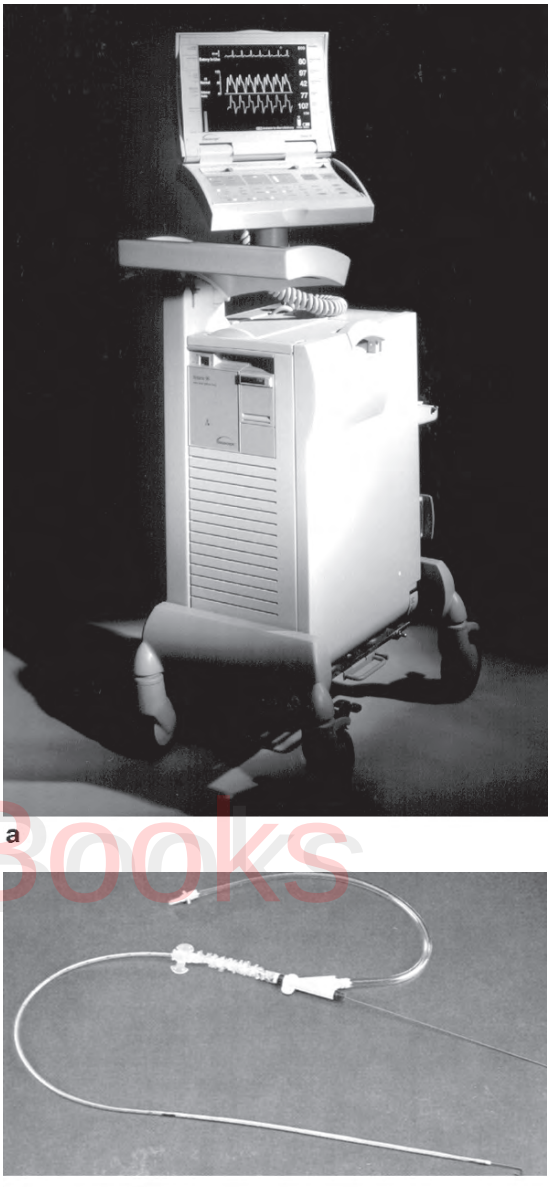


FIGURE 7.2. Intraaortic balloon pump (Datascope System 98/98XT, Datascope Corporation, Fairfield, NJ). (A) Console for the IABP. (B) Catheter-mounted balloon is typically placed into the thoracic aorta through a percutaneous insertion in the groin.

a catheter-based balloon that produced hemodynamic effects similar to the Harken pump, but without an extracorporeal pump.[27] Moulopolous passed a balloon into the aorta that inflated during ventricular diastole, thereby augmenting diastolic blood pressure. Deflation just before ejection effectively

DropOnBooks

decreased the heart afterload and thus the work of the heart during systole.

The major hemodynamic effects of the IABP are a decrease in left ventricular afterload and an increase in coronary artery perfusion pressure. Cardiac output improves from enhanced myocardial contractility as a result of increased coronary blood flow and reduced afterload and preload. The IABP is positioned with the tip of the balloon lying just distal to the left subclavian artery. The balloon should fill the aorta so that during the inflation cycle it nearly occludes the vessel. In adults, balloon volumes of 30–40 ml are optimal. Inflation should be timed to coincide with closure of the aortic valve, which is obtained by identifying the dicrotic notch of aortic blood pressure trace (Figure 7.3). Deflation should occur as late as possible to maintain the duration of the augmented diastolic blood pressure but before the aortic valve opens and the ventricle ejects. Deflation is timed to occur with the onset of the electrocardiographic R wave. A regular heart rate with an easily identified R wave or a good arterial pulse tracing with a discrete aortic dicrotic notch optimizes performance of the IABP. Current IABP consoles trigger off the electrocardiographic R wave or from the arterial pressure tracing. During tachycardia, the IABP is usually timed to inflate every other beat. In unstable patients, obtaining a regular rhythm or regular paced rhythm optimizes proper timing of the IABP.

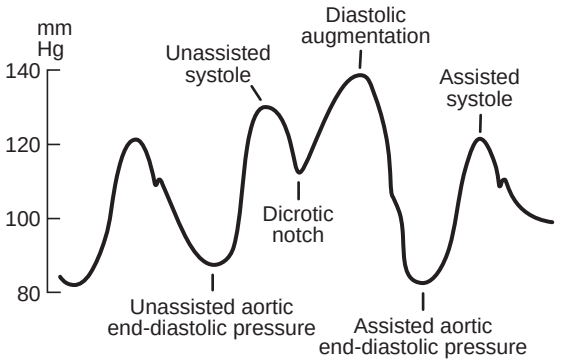


Figure 7.3. Aortic pressure tracing during IABP support. With correct timing, balloon inflation begins immediately after aortic valve closure, signaled by the dicrotic notch. Compared with unassisted ejection, the pump augments diastolic blood flow by increasing peak aortic pressure during diastole (diastolic augmentation). Balloon deflation before systole decreases ventricular afterload, with lower aortic end-diastolic pressure (assisted aortic end-diastolic pressure) and lower peak systolic pressure (assisted systole).

The IABP can be inserted into the common femoral artery either by the percutaneous technique using a modified Seldinger technique, or by surgical cut-down. A cut-down is generally performed during cardiopulmonary bypass when the arterial pulse is absent because of nonpulsatile flow. In situations where the common femoral or iliac arteries cannot be used because of occlusive disease and an inability to advance the guide wire, the axillary artery, exposed below the middle third of the clavicle, may be used as an alternative entry site. Alternatively, in situations of postcardiotomy failure to wean, the ascending aorta may be utilized as an insertion site. Fluoroscopy or transesophageal echocardiography should be utilized to ensure proper positioning of the guide wire. The balloon should be positioned so that during inflation it does not occlude the left subclavian artery. Heparin is recommended if the IABP will remain in place for more than 24 h. Weaning of the IABP entails observing the clinical response to reducing the ratio of assisted heartbeats to total beats from 1:1 to 1:3 or 1:4.

Complications from use of the IABP include leg ischemia, balloon rupture, thrombosis within the balloon, sepsis, infection at the insertion site, bleeding, false aneurysm formation, lymph fistula, femoral neuropathy, vessel perforation with hemorrhage, and aortic dissection from catheter passage below the intima. The largest study to date of complications from IABP therapy from the Benchmark Registry included 16,909 patients from 243 institutions in 18 countries.[30] In this registry, the mean age of the patients was 66 years and only 12% had previously documented peripheral vascular disease. Approximately 80% of the IABPs were inserted with an arterial sheath and 78% used a 9.5 Fr instead of the smaller 8 Fr-size catheter. IABP-related mortality was 0.05% (Table 7.3). The prevalence of any limb ischemia was 2.9% and that of major limb ischemia was 0.9%. The need for amputation from IABP insertion was 0.1%. Multivariate analysis revealed that female sex, age, peripheral vascular disease, and body surface area predicted procedure complications (Table 7.3). Smaller IABP catheter size (8 Fr) is associated

TABLE 7.3. Complication rates and predictors of adverse events utilizing IABP therapy from the Benchmark Registry

Complication incidence (%) (n = 16,909 patients)		
IABP-related mortality	0.05%	
Any limb ischemia	2.9%	
Major limb ischemia	0.9%	
Severe access site bleeding	0.8%	
Amputation	0.1%	
Balloon leak	1.0%	
Multivariate predictors of IABP complications		
	Odds ratio	p value
Peripheral vascular disease	1.97	<0.001
Female	1.74	<0.001
Body surface area <1.65 m^2	1.45	<0.05
Age >75 years	1.29	<0.05

Source: Adapted from Ferguson et al.[30] In this study, major limb ischemia was defined as a loss of pulse or sensation, or pallor requiring vascular surgery. Minor limb ischemia was defined as loss of pulse that resolved with the removal of the IABP. Major bleeding was defined as bleeding causing hemodynamic compromise requiring blood transfusion or vascular surgery. Mortality due to IABP was defined as death due to vascular perforation or embolism related to the IABP procedure.

with a lower rate of ischemic complications and sheathless insertion may be associated with a lower ischemic complication rate as well.

The IABP has several disadvantages. In the best of circumstances, cardiac output is augmented by 25% as compared to LVADs that can augment cardiac output by three to five times baseline flows. The IABP offers no significant support to the right heart. Mobilization and ambulation of the patient is limited while the IABP is being utilized. IABP are generally contraindicated in the presence of significant aortic insufficiency (increases diastolic pressure and regurgitant volume), aortic aneurysm and/or dissection, and sepsis.

7.5.2. Extracorporeal Membrane Oxygenation

Extracorporeal membrane oxygenation [ECMO; also known as extracorporeal life support (ECLS)] utilizes a modified heart–lung machine to provide circulatory assistance as well as oxygenation and carbon dioxide removal from blood for days to weeks to permit recovery from severe cardiac and/or pulmonary failure[31–34] (Figure 7.4). The ECMO circuit is similar in concept to the cardiopulmonary bypass circuit routinely used in the operating room, but has certain modifications, particularly the

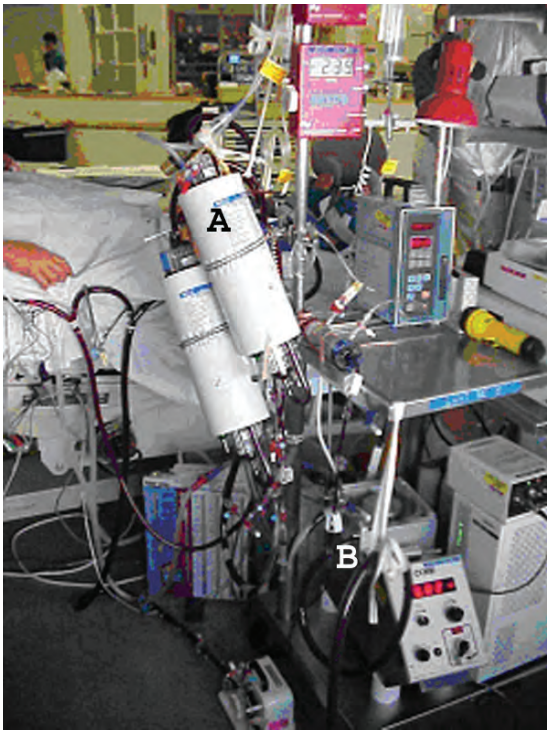


FIGURE 7.4. Photograph of an extra-corporeal membrane oxygenation (ECMO) circuit utilized at the University of Michigan. [Note: roller pump, bottom center of the photograph (B), and membrane oxygenator, center of the photograph (A)]. Photograph courtesy of Dr. Fresca Swaniker, Department of Surgery, Division of Surgical Critical Care, University of Michigan.

inclusion of membrane oxygenators, that permit extended periods of support. The first successful use of prolonged ECMO was reported by Hill in 1972.[35] ECMO has been used in an increasing number of indications including neonatal, pediatric, and adult respiratory support, postcardiotomy support, and as a bridge to an implantable LVAD ("bridge to bridge concept") or bridge to heart transplantation.[36–38]

ECMO circuits are composed of a centrifugal pump with either hollow fiber or membrane oxygenator, oxygen blender, pump console, heat exchanger, and pump cart. A roller pump along with membrane oxygenator is preferred by some centers.[34] Heparin-bonded circuits are also utilized. These circuits reduce but not eliminate the need for systemic anticoagulation and may reduce the inflammatory response associated with ECMO.

DropBooks

Cannulation for ECMO is extremely variable and depends on the clinical situation and whether a venoarterial or venovenous circuit is desired. Venovenous circuits are the preferred method for providing respiratory support, while venoarterial circuits can be utilized for either cardiac and/or respiratory support. In emergent situations where institution of circulatory support is needed within minutes, percutaneous cannulation of the femoral vein and artery can be performed. In less urgent situations, cut-down on the internal jugular and carotid artery or respective femoral vessels can be performed. In cases of postcardiotomy failure in the operating room, venous access can be obtained by insertion of a cannula in the right atrium and arterial outflow obtained by cannulation of the ascending aorta.

ECMO support significantly unloads the right ventricle but does not satisfactorily unload the left ventricle, although left ventricular preload is reduced by decreasing pulmonary venous return. In patients with severe left ventricular dysfunction, left ventricular distention and subsequent development of significant pulmonary hypertension may result in pulmonary hemorrhage. The use of an IABP may help to reduce left ventricular afterload during systole and improve myocardial contractility, in addition to providing pulsatile flow. The use of the IABP and inotropic therapy can maintain sufficient cardiac contractility to prevent ventricular distension and thrombus formation. If application of an IABP does not effectively relieve ventricular distension and pulmonary hypertension, an atrial septostomy can be performed to vent pulmonary venous return.[36,37] Alternatively, a left-sided vent can be connected to the venous line of the ECMO circuit to relieve ventricular distention. It is important during ECMO support to maintain some degree of pulmonary blood flow to prevent thrombosis. It is important to continue ventilation of the lungs to maintain the oxygen saturation of the blood ejected from the left ventricle above 90%. Poorly oxygenated blood ejected from the left ventricle will perfuse the coronary arteries and the cerebral circulation and may result in hypoxic injury to the heart and brain.

To promote recovery of respiratory function, it is important to manage the patient utilizing low pressure and oxygen ventilator settings to avoid ventilator-induced injury, pressure-controlled ventilation, hemofiltration to dry weight, intermittent prone positioning, and nutritional support. Right atrial and left atrial pressures as well as pump flows are monitored, and mixed venous saturations are maintained above 75%, which is an accurate reflection of the adequacy of systemic flows. A sudden decrease in venous drainage is usually manifested by chugging of the venous lines with wide respiratory fluctuations and flow. Causes include hypovolemia, kinking or malposition of the cannulae, pneumothorax, and pericardial tamponade.

Numerous large clinical series have reported successful use of ECMO for cardiac and/or respiratory support in adult, pediatric, and neonatal patients. In the largest series reported to date, Bartlett and colleagues at the University of Michigan reported on the outcome of 1,000 patients supported with ECMO from 1980 through 1998.[34] Survival to hospital discharge was 88% for 586 cases of neonatal respiratory failure, 70% for 132 cases of respiratory failure in children, and 56% for 146 cases of respiratory failure in adult patients. Venovenous ECMO was the preferred method of respiratory support since 1988. For patients with cardiac failure, 33% of adult patients (31 cases) and 48% of pediatric patients (105 cases) survived to hospital discharge. Survival in adult patients was improved by utilizing ECMO as a bridge to longer-term implantable devices in patients who did not demonstrate early recovery of myocardial function.[36,37] Conversely, the availability of long-term implantable devices has extended the use of ECMO in situations where recovery of myocardial function is unlikely.[36–38] Smedira and colleagues reported on the clinical experience of 202 adult patients receiving ECMO for cardiac failure at the Cleveland Clinic.[39] Survival at 24 h, 30 days, and 1 year was 90%, 38%, and 29%, respectively. For patients alive at 30 days, survival at 5 years was 63%. Complications occurring during ECMO support were significant. Infectious complications occurred in 49% of patients. Forty percent of patients required dialysis, neurologic complications occurred in 33%, and limb complications occurred in 25%. Risk factors for death included older age, thoracic aortic operations, reoperations, decompensated heart failure, and nonuse of an IABP. Magovern and colleagues reported on the outcome of 92 adult patients following institution of ECMO support.[40] Twenty of 55 (36%) patients survived

to hospital discharge following ECMO support for postcardiotomy failure to wean. Twenty-three of 27 (85%) patients survived ECMO support following percutaneous interventions in the catheterization laboratory while two of four (50%) survived ECMO for primary cardiac allograft failure. No patient ($n = 6$) survived ECMO support for cardiac resuscitation.

7.5.3. Extracorporeal, Rotary Pump with Centrifugal Flow Design

7.5.3.1. TandemHeart Percutaneous Ventricular Assist Device

The TandemHeart Percutaneous Ventricular Assist Device (pVAD) (Cardiac Assist Technologies, Inc., Pittsburgh, PA) is a percutaneous left atrial to femoral artery VAD (Figures 7.5 and 7.6). The pump is a low speed, continuous flow, centrifugal pump that has a very low potential for hemolysis and thromboembolism. It is a dual-chamber pump composed of an upper housing and a lower housing assembly. The upper housing provides a conduit for inflow and outflow of blood. The lower housing assembly provides communication with the controller, the means for rotating the impeller of the VAD, and an anticoagulation infusion line integral to the pump to provide a hydrodynamic bearing, cooling of the bearing, and local anticoagulation. The controller is a microprocessor-based electromechanical drive and infusion system that is designed to operate on AC current or on internal batteries.

Implantation of the device is performed percutaneously through the right femoral vein (Figure 7.6). A standard Brockenbrough catheter is inserted into the superior vena cava and the interatrial septum is punctured in the fossa ovalis using a Ross needle. The Brockenbrough catheter is then exchanged for a stiff guide wire with a distal soft wire loop identical to the device used for mitral valvuloplasty by the Inoue method. The transseptal puncture site is then dilated to 21F with a 2-stage dilator followed by insertion of a venous inflow cannula, which is sutured to the skin of the thigh. An arterial perfusion catheter of 14F–19F is inserted percutaneously into the right femoral artery or two arterial perfusion catheters of 12F into both femoral arteries.

DropBooks

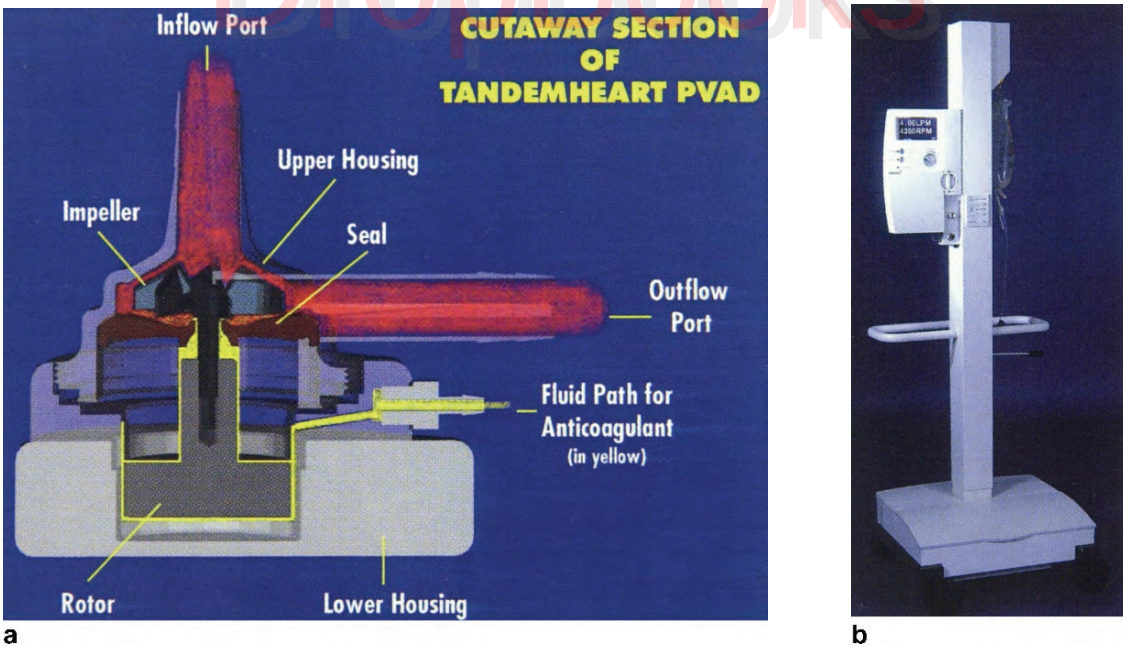


FIGURE 7.5. (A) TandemHeart pVAD centrifugal pump (CardiacAssist, Inc., Pittsburgh, PA). (B) Electrical control console for the TandemHeart pVAD centrifugal pump.

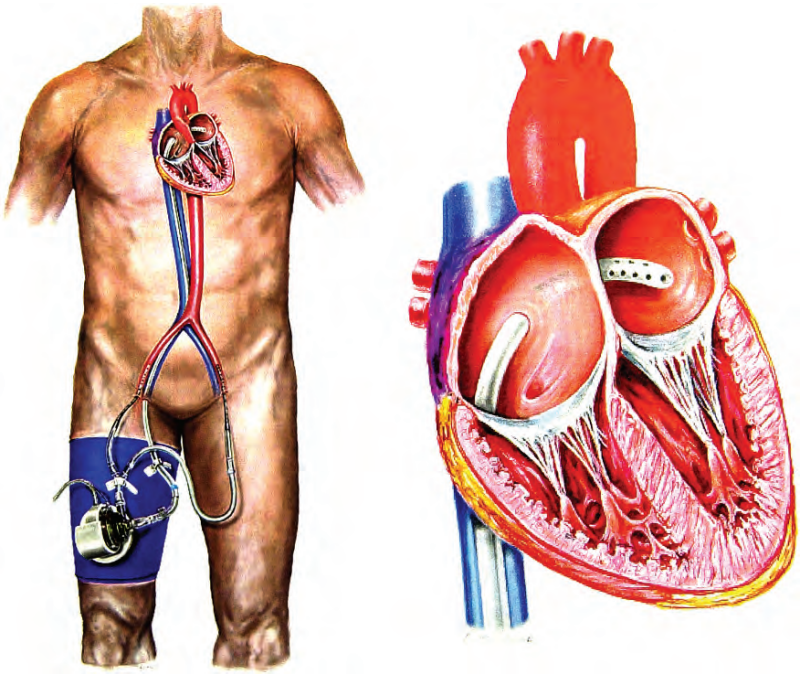


FIGURE 7.6. Schematic representation of the cannulation of the femoral artery and femoral vein with transeptal placement of the inflow catheter within the left atrium from the femoral vein. The TandemHeart pVAD is secured to the patient's right thigh.

Thiele and colleagues reported on the use of the TandemHeart pVAD in 18 patients presenting with cardiogenic shock.[41] Mean duration of support was 4 ± 3 days. Following percutaneous placement of the device, mean cardiac index improved from 1.7 ± 0.3 L/min/m^2 to 2.4 ± 0.6 L/min/m^2. Mean device flow during support was 3.2 ± 0.6 L/min. Pulmonary wedge pressure decreased from 31 ± 8 mmHg to 23 ± 6 mmHg. Survival at 30 days was 56%. The TandemHeart is currently completing a multicenter, Phase II, FDA trial to examine effectiveness for patients presenting with acute cardiogenic shock.

7.5.4. Extracorporeal, Rotary Pump with Axial Flow Design

7.5.4.1. Impella VAD

The Impella Recover® system (Impella Cardiosystem AG, Germany) is a miniaturized impeller pump located within a catheter. The device can provide support for the left side of the heart using either the Recover LD 5.0 (implanted via direct placement into the left ventricle) or the Recover LP 5.0 LV (placed percutaneously through the groin and positioned in the left ventricle) or the right side of the heart using the Recover RD (Figure 7.7). The microaxial pump of the Recover LD/LP 5.0 can pump up to 4.5 L/min at a speed of 33,000 rpm. The pump is located at the distal end of a 9-Fr catheter. At its largest outside diameter, which contains the pump housing, the Impella Recover measures 21 Fr. The catheter shaft contains the electrical connections for the pump motor and sensor as well as for a separate tube used for transfer of purged fluid.

In an early multicenter trial, Siegenthaler and colleagues reported on the outcomes of 24 patients treated with the Impella Recover system (16 in conjunction with IABP) compared to 198 historical controls treated with IABP support and matched for clinical acuity utilizing three risk assessment scales.[42] Mortality for Impella patients was 54% (13 out of 24), similar to that for high-risk IABP patients [Hausmann score ≥ 2 (57%), intensive care unit score ≥ 2 (51%), Texas Heart Institute score ≥ 0.75 (55%), and cardiac index ≤ 2.3 (45%)]. Pump flow was 3.3 ± 0.7 L/min at 28,000 ± 4,500 rpm.

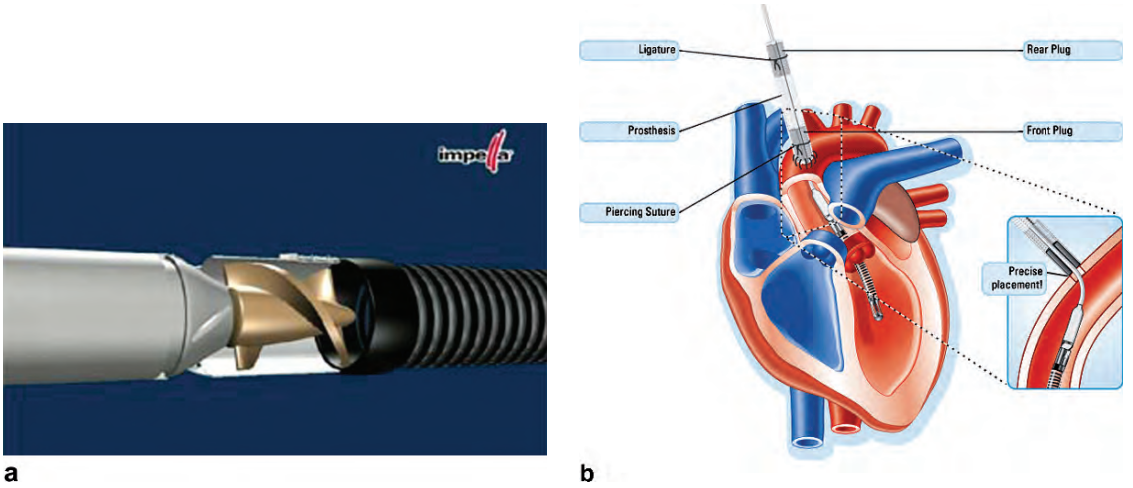


FIGURE 7.7. The Impella Recover System (Impella Cardiosystem AG, Germany). (A) A diagrammatic view of the microaxial impeller within the catheter of the Impella Recover System. (B) Diagrammatic view of the placement of the Impella Recover System across the aortic valve.

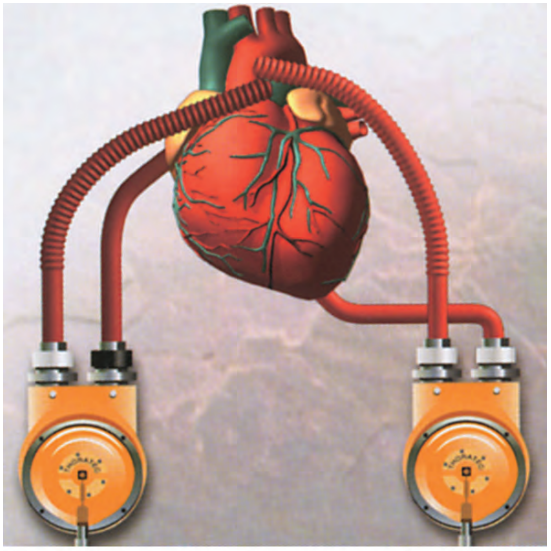
Support time was 61 ± 56 h (range, 7–228 h). Four devices required repositioning. One device failed (leaking purge line) and was removed. Hemolysis was minimal (LDH 540 ± 260 U/dl for Impella survivors). Importantly, Impella patients able to increase their cardiac output to 1 L/min or more above the pump flow of the Impella Recover had a 10% (1 out of 10) mortality, versus 88% (8 out of 9) in patients with a residual cardiac function of 1 L/min or less (p = .001). Meyns and colleagues reported on 16 patients (6 percutaneously via the femoral artery and 10 directly through the aorta) undergoing support with the Impella Recover system.[43] Average pump flows were 4.24 ± 0.28 L/min. Mean blood pressure before Impella support was 57.4 ± 13 mmHg, which increased to 74.9 ± 13 mmHg after 6 h and 80.6 ± 17 mmHg (p = 0.003) after 24 h. Cardiac output increased from 4.1 ± 1.3 L/min to 5.5 ± 1.3 L/min (p = 0.003) and 5.9 ± 1.9 L/min (p = 0.01) at 6 and 24 h, respectively. Mean pulmonary wedge pressure decreased from 29 ± 10 mmHg to 17 ± 5 mmHg and 18 ± 7 mmHg (p = 0.04) at 6 and 24 h, respectively. Device-related complications included three sensor failures (no clinical action), one pump displacement (replacement), and six incidences of hemolysis (peak free plasma hemoglobin level > 100 mg/dl, no clinical action). Eleven patients (68%) were weaned and six (37%) survived to discharge.

7.5.5. Extracorporeal, Pulsatile Devices

7.5.5.1. Thoratec Ventricular Assist System

The Thoratec Ventricular Assist System (VAS) (Thoratec Laboratories, Inc., Pleasanton, CA) is a paracorporeal, pneumatically powered, pulsatile system configured for univentricular or biventricular support that consists of a seamless polyurethane blood sac contained within a rigid polycarbonate housing[44,45] (Figure 7.8). An external drive console sends pressurized air to the pump, which compresses the blood sac and causes blood to be ejected. Bjork-Shiley concavo–convex tilting-disk valves within the inflow and outflow conduits ensure unidirectional blood flow. The device has a stroke volume of ~65 ml and a maximum output of 7 L/min. For left ventricular support, the pump inflow cannula can be placed in the left ventricular apex or the left atrium, and the pump outflow conduit is anastomosed to the ascending aorta. For right ventricular support, a large-bore cannula is placed in the right atrium, and the outflow conduit is sewn to the main pulmonary artery. After the cannulae have been externalized subcostally, the inflow and outflow cannulas are connected to the pump(s), which reside externally on the anterior surface of the abdomen. During the support period, anticoagulation with dextran, heparin, warfarin, and dipyridamole is required. Patients may be ambulatory but their mobility is limited by the size of the

DropBooks



a



b

FIGURE 7.8. The Thoratec VA (Thoratec Laboratories, Inc., Pleasanton, CA). (A) Schematic representation of the cannulation sites for biventricular support. (B) Thoratec VAS extracorporeal pneumatic blood pump.

drive console and the paracorporeal position of the pump(s). The Thoratec VAD can be operated in fixed-rate, volume, or synchronous mode. The FDA has approved the Thoratec VAS for use as a bridge to recovery and bridge to transplantation. It is currently the only extracorporeal system with approval as a bridge to heart transplantation. Thus, in situations where patients fail to recover myocardial function, the device can provide circulatory support until heart transplantation, if indicated. New system designs to the paracorporeal Thoratec VAS currently include a small, portable drive console that enhances patient mobility and permits discharge from the hospital.[46]

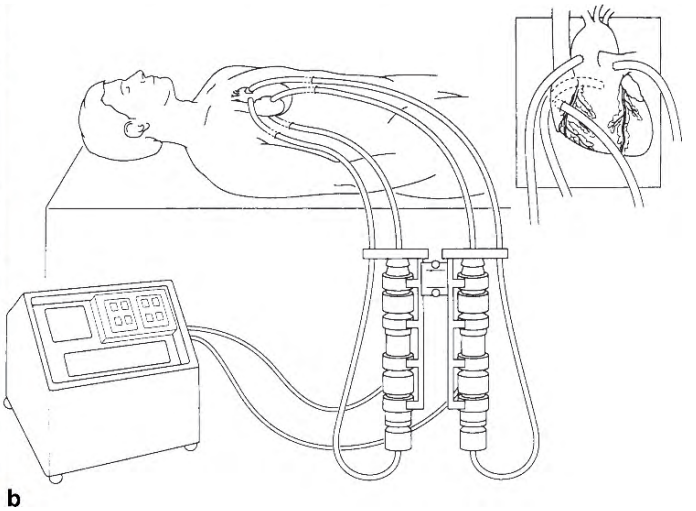
McBride and colleagues reported on the outcomes of 111 patients supported with the Thoratec VAS for acute cardiac failure.[44] Survival at 1 year was ~25% for 44 patients treated with the intent to recover. This compared to ~58% 1-year survival for 67 patients treated with the intent to bridge to transplant. The duration of support ranged from 0.1 to 27 days (mean 4.5 days) in the recovery group and from 0.2 to 184 days (mean 40.7 days) in the bridge to transplantation group. Complications were significant in both groups. In 104 patients bridged to transplantation with the Thoratec VAS, El-Banayosy and colleagues reported a survival to transplant of 61%.[45] Approximately 50% of the patients required biventricular support and outcomes were worse for this group. Age, preimplant ventilator use, and higher preimplant total bilirubin were significant predictors of adverse outcome.

7.5.5.2. Abiomed BVS 5000

The Abiomed BVS 5000 (Abiomed, Inc., Danvers, MA) support system is an automated ventricular support device intended to provide temporary uni- or biventricular support[7–9,47,48] (Figure 7.9). The Abiomed BVS 5000 was the first FDA-approved device for short-term extracorporeal circulatory support as a bridge to recovery in cases of cardiogenic shock due to postcardiotomy failure to wean, acute myocarditis, and myocardial infarction. Positioned externally, this pulsatile system simulates normal physiologic mechanical cardiac function. A microprocessor-based drive console is used to supply power to a disposable, pneumatically driven two-chambered blood pump that supports one side of the heart. Left atrial blood



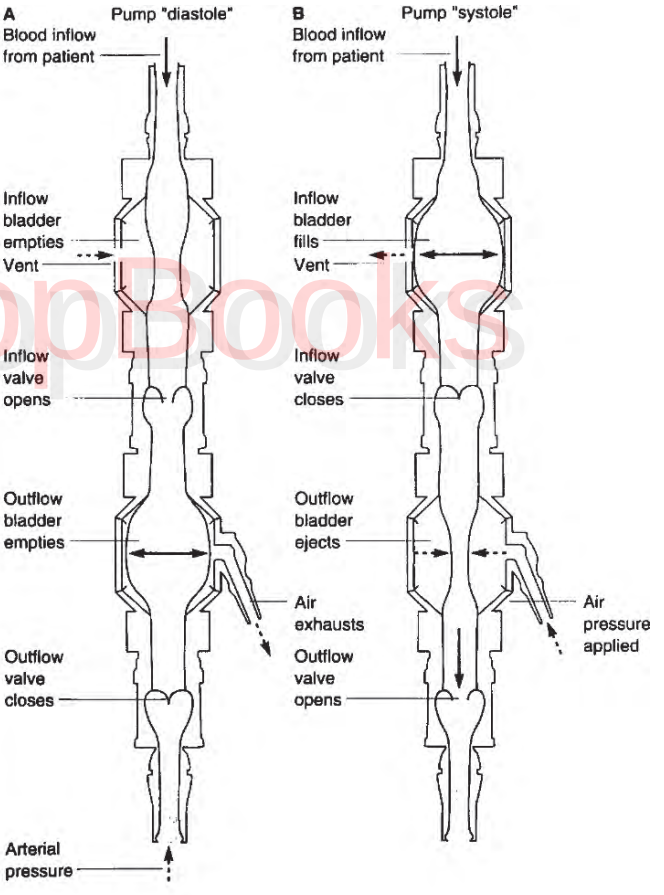
a



b



c



DropBooks

FIGURE 7.9. **A** The pneumatic drive console and blood pumps for the Abiomed BVS 5000 biventricular assist device (Abiomed, Inc., Danvers, MA). **B** Schematic representation of the cannulation sites for biventricular support and patient and device position for the Abiomed BVS 5000. (Reproduced with permission from Pagani and Aaronson.[49(p1516)]) **C** Photograph and schematic diagram of the Abiomed blood pumps. (Reproduced with permission from Pagani and Aaronson.[49(p1517)]).

inflow is returned to the ascending aorta and right atrial inflow is returned to the pulmonary artery. Transthoracic cannulae are used to connect the external system with the patient. Each blood pump consists of two Angioflex polyurethane atrioventricular-like chambers. Trileaflet polyurethane valves are strategically positioned to separate (1) atrial and ventricular bladders and (2) ventricular bladders and outflow cannulae. One or two disposable blood pumps are operated by a single BVS console, which automatically adjusts beat rate and systolic/diastolic ratio based on compressed air flow into and out of the external system. The pump is placed at the bedside and blood drains from the patient's left or right atrium by gravity, without the use of vacuum pressure, into the top of the pump and returns to the patient's aorta or pulmonary artery from the bottom of the pump. Filling of the blood pump chambers can be regulated by adjusting the height of the blood pump relative to the patient's heart. The blood pump is a dual-chamber device that incorporates an atrial (filling) chamber and a ventricular (pumping) chamber. Unidirectional flow is ensured by two trileaflet polyurethane valves fabricated from Angioflex, a biomaterial. The durations of pump systole and diastole are calculated automatically by the microprocessor to optimize pump filling and maintain a stroke volume of 83 ml. The console drives and adjusts left and right sides independently of each other. System controls are essentially limited to "on" and "off." In addition to the traditional blood pumps and console, new blood pump designs and console, designated the AB5000, have recently been introduced and approved by the FDA for short-term circulatory support (Figure 7.10).

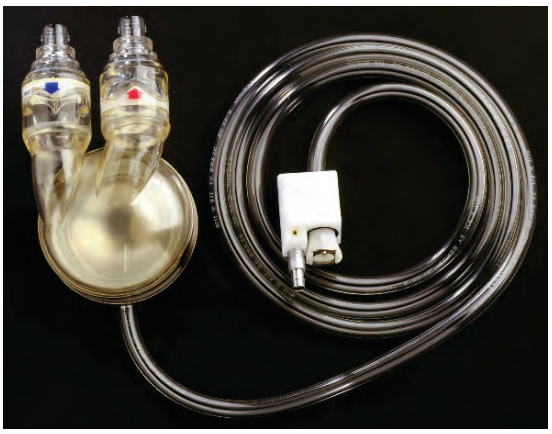


FIGURE 7.10. Abiomed AB5000 blood pump design.

In a 6-year experience from the Hahnemann University Hospital, Samuels and colleagues reported on the outcomes of 45 patients supported with the Abiomed BVS 5000.[9,48] Overall, 22 (49%) patients weaned from support and 14 (31%) survived to hospital discharge. For patients who received optimal timing of insertion by establishing a weaning algorithm, outcomes were improved, with 60% of patients weaning from device support and 43% surviving to hospital discharge (Figure 7.1 and Table 7.1).

7.5.6. Implantable, Pulsatile Flow Devices

7.5.6.1. HeartMate XVE LVAD

The HeartMate XVE LVAD (Thoratec Laboratories, Inc., Pleasanton, CA) is an implantable, pulsatile LVAD designed for long-term circulatory support and is approved by the FDA as a bridge to heart transplantation and destination therapy[49–53] (Figure 7.11). The unique feature of this device is that its blood-contacting surfaces of the pump are textured with sintered titanium spheres on the rigid surface and integrally textured polyurethane on the movable surfaces to encourage the deposition of circulating cells (Figure 7.11). The interior surfaces of this LVAD have been textured using sintered titanium microspheres on the rigid metallic surfaces and integrally textured polyurethane on the movable diaphragm. This design feature permits a uniform autologous tissue lining to establish on all the blood-contacting surfaces of the pump, minimizing thrombus formation and bacterial colonization. The tightly adherent fibrin–cellular matrix, once mature, contains macrophages, mesenchymal cells, endothelial cells, and other blood components. This densely adherent neointima eliminates direct contact between the device and blood elements, substantially reducing the risk of peripheral embolization. In addition to the unique surface design, the pusher plate of the pump moves the diaphragm in a way that creates a wandering vortex in the blood chamber. This feature prevents stagnation of blood in any part of the chamber. The HeartMate blood pump consists of a flexible polyurethane diaphragm within a ridged outer titanium alloy



a



b

FIGURE 7.11. **A** The HeartMate XVE LVAD (Thoratec Laboratories, Inc., Pleasanton, CA). **B** The HeartMate XVE LVAD demonstrating the textured surfaces of the metal housing and diaphragm surfaces. The interior surfaces of this LVAD have been textured using sintered titanium microspheres on the rigid metallic surfaces and integrally textured polyurethane on the movable diaphragm.

housing. The inflow and outflow conduits of the HeartMate device each contain a 25-mm porcine valve within a titanium cage to ensure unidirectional blood flow. The outflow conduit is extended by a 20-mm woven Dacron graft. With the XVE LVAS, diaphragm movement and blood ejection depend on an electric motor positioned below the diaphragm (Figure 7.12). The electric rotary motor within the titanium housing drives a cam up and down (translational movement) causing diaphragm movement. An external vent equalizes the air pressure and permits emergency pneumatic actuation in the event of electrical failure. The external system controller and batteries in the XVE LVAS are small and lightweight, allowing the patient nearly unlimited mobility. The drive line is covered with a polyester velour that promotes tissue bonding and anchoring to the skin and reduces the risk of infection. The XVE LVAS is powered by two rechargeable batteries that provide 4–6 hours of charge and are usually worn in a shoulder holster, vest, or belt. The wearable electrical devices currently available have external backup mechanisms to continue support without the need for reoperation in case of failure of the device. If the device should fail, the native heart is able to provide systemic support until the device can be examined. Because the electronic control unit is outside the body, it can easily be repaired should failure of the software, chip, or electronics occur. Finally, if the motor device fails, the single-pusher-plate device can be pneumatically activated with a hand-held portable pump or with a pneumatic console.



FIGURE 7.12. The HeartMate XVE LVAD demonstrating the internal rotary motor that drives the movable diaphragm.

The maximum pump flow is 9.6 L/min for the XVE LVAS. The HeartMate device can be operated either in a fixed-rate mode or, more often, in an automatic mode that more closely resembles normal physiologic conditions. In the automatic mode, the device ejects when the pump is 90% full or when it senses a decreased rate of filling. As the patient's activity increases, the pump fills faster and the rate (or stroke volume) automatically increases, resulting in an increase in pump output. With a decrease in activity, pump filling and output decrease. Because the aortic valve rarely opens when the heart is fully

supported by an LVAD, pump output is synonymous with cardiac output. During normal operation, the pump completely unloads the left ventricle and supports cardiac output at physiological levels. Because of the portability and ease of operation of the HeartMate XVE LVAS, patients can be discharged to await heart transplantation outside the hospital.

7.5.6.2. Novacor LVAS

The Novacor LVAD (WorldHeart, Inc., Ottawa, Canada) is a portable, implantable LVAD designed for long-term circulatory support and is approved by the FDA for bridge to transplant indication[54–56] (Figure 7.13). The Novacor is currently undergoing clinical investigation for destination indication in the RELIANT trial. The Novacor LVAD differs significantly from the HeartMate XVE LVAD in its mode of pump actuation and use of smooth blood-contacting surfaces. During pump systole, two opposing pusher plates compress a seamless polyurethane blood sac, causing ejection of blood. Unidirectional flow is ensured by use of 21-mm bioprosthetic valved conduits at the inlet and outlet orifices. The device produces a maximum stroke volume of 70 ml and is monitored by an external drive console. An internal solenoid converts the electric energy from the console to mechanic energy, compressing the pusher plates and pressurizing the pump sac for blood ejection. A percutaneous lead contains the necessary electrical wires and a vent to transfer air. In 1993, the Novacor LVAS was converted from a console-operated system into a wearable system to enhance patient mobility. The wearable system eliminates the need for a bulky console by incorporating a compact controller and rechargeable power packs that are worn on the patient's belt. The wearable system is designed for out-of-hospital use and can be monitored with a bedside monitor. The external controller provides power and allows control and monitoring of the pump. The system can be operated in either a fixed-rate, synchronous, or fill-to-empty mode. The synchronized mode maximizes cardiac unloading. In this mode, an electrocardiographic signal causes pump diastole to correspond with cardiac systole, allowing the heart to fill the pump with little effort. Alternatively, pump output may be maximized by means of the fill-to-empty mode in which the pumping rate is adjusted automatically depending on the filling rate of the pump. Third, the system may be operated in a fixed-rate mode in which the operator sets a constant pumping rate. During device use, anticoagulation with heparin and later with warfarin and antiplatelet therapy is necessary to prevent thromboembolism. During long-term support, ambulatory patients can be discharged and live outside the hospital while awaiting a suitable donor heart.



FIGURE 7.13. Novacor LVAD (WorldHeart, Inc., Ottawa, Canada).

7.5.6.3. Thoratec Implantable VAD

The Thoratec implantable VAD (IVAD) (Thoratec Laboratories, Inc., Pleasanton, CA) is a small, simple, and versatile IVAD based on the paracorporeal Thoratec VAS. It has recently been developed and approved for circulatory assist as a bridge to heart transplantation or recovery[57] (Figure 7.14). The IVAD has the same blood flow path and Thoralon polyurethane blood pumping sac as the paracorporeal Thoratec VAS, but the housing is a smooth contoured, polished titanium alloy. The IVAD has a new sensor to detect when the pump is full and empty, and is controlled with the Thoratec TLC-II portable VAD driver, which is a small, briefcase-sized, battery-powered, pneumatic control unit. A small flexible (9-mm outer diameter) percutaneous pneumatic driveline for each VAD is tunneled out of the body from the LVAD or right ventricular assist device (RVAD) in a pre- or intraperitoneal position. Small size and simplicity are the major advantages of the new device. The IVAD weight (339 g) and implanted volume (252 ml) are approx-

imately one-half that of the current implantable pulsatile electromechanical LVAD systems.

7.5.7. Implantable, Rotary Pumps with Axial Flow Design

There are currently three rotary pumps with axial flow design in clinical trials in the USA. These three devices share a common design that consists of an internal impeller supported by bearings at the inlet flow straightener and outlet diffuser. The movement of the impeller is achieved by an electric current and magnetic field induced by the motor stator (Figure 7.15).

7.5.7.1. HeartMate II

The HeartMate II LVAD (Thoratec Laboratories, Inc., Pleasanton, CA) is a small integrated pump-motor assembly that connects into the circulatory system through an apical cannula whose inlet orifice draws blood flow from the left ventricular apex, and an outflow cannula that is anastomosed to the ascending aorta[58–60] (Figure 7.16). The pump consists of a 12-mm diameter straight duct and uses 14-mm diameter grafts for both the inlet and outlet cannulae. Upon entering the pump, blood passes through inlet stator vanes. After exiting the stator vanes, the blood flow is energized by the pump rotor that imparts tangential velocity and kinetic energy. Blood flow leaving the rotor then passes through a set of exit stator vanes that turn and diffuse the stream velocity, recovering kinetic energy in the process. The net action results in generation of a net pressure rise across the pump. Torque required to drive the pump rotor is developed by an integral electric motor. The pump's 12-mm diameter duct is actually a thin-walled tube that passes through the bore of the motor's coil windings. The motor's rotor is a permanent magnet located in the hub of the pump's rotor. The location of the pump rotor in the tube places the motor magnet in the proper position with respect to the coils, which is at the centerline of the winding's axis, and centered longitudinally with respect to the coil's length. Excitation current sequentially commutated to the coils creates a spinning magnetic field, thereby imparting torque and angular velocity to the motor magnet. The pump rotor spins on two bearings located at either end. Both bearings react against radial and axial thrust forces. Each bearing's stationary element is located in the hub of the respective inlet and outlet stators; the bearings themselves are similar to standard ball-cup jewel bearings. The outer boundary of the bearing's adjacent static and moving surfaces is washed directly by the main blood flow. Under normal operation, inlet pressure to the axial flow pump will be cyclic and vary with the systolic–diastolic phases of the left ventricle. Pressures developed within the left ventricle during systole depend upon cardiac contractility and the overall flow demand of the patient. In the clinical situation of compromised cardiac contractility, with the pump operating at some nominal speed, systolic contractions of the heart will generate a pressure rise at the pump inlet, followed during diastole, by inlet pressures falling to its lowest level. This leads to a changing differential pressure across the pump, which in turn causes a corresponding fluctuation of flow delivered to the aorta. Thus, under most cir-



FIGURE 7.14. Thoratec IVAD (Thoratec Laboratories, Inc., Pleasanton, CA).

DropBooks

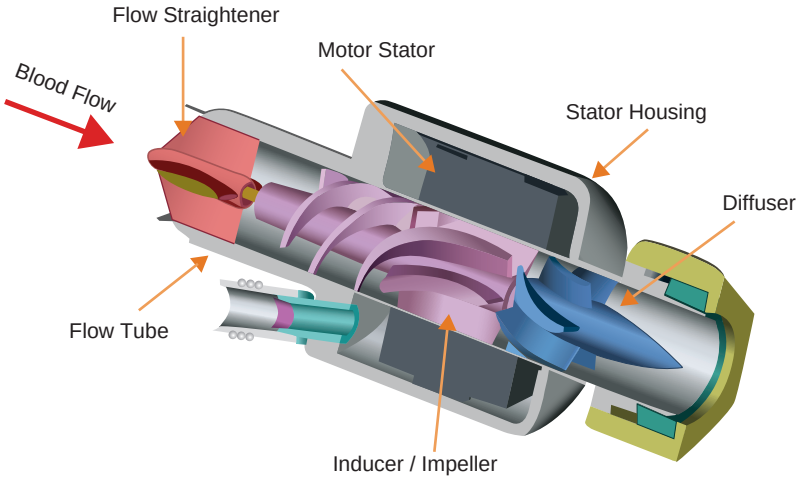


FIGURE 7.15. Rotary pump with axial flow design.



FIGURE 7.16. A HeartMate II LVAD (Thoratec Laboratories, Inc., Pleasanton, CA). B Jarvik 2000 LVAD (Jarvik Heart, Inc., New York, NY). C DeBakey LVAD (MicroMed, Inc., Houston, TX).

cumstances, the rotary pump will generate some pulsatility. Totally nonpulsatile flow would occur if the heart is in fibrillation, a state that cannot be tolerated chronically, or if the pump is operated at too high a speed or negative inflow pressure causing left ventricular collapse. The HeartMate II is currently in human testing.

7.5.7.2. Jarvik 2000

The Jarvik 2000 LVAD (Jarvik Heart, Inc., New York, NY) is a compact axial flow impeller pump[61–65] (Figure 7.16). The outflow orifice of the pump is attached to a Dacron graft for anastomosis to the descending thoracic aorta. The Jarvik 2000 pump is inserted through a sewing cuff sewn into the apex of the left ventricle. The current adult version of the Jarvik 2000 measures 2.5 cm in diameter by 5.5 cm in length, with a weight of 85 g and a displacement volume of 25 ml. The pediatric iteration of the device measures 1.4 cm in diameter by 5 cm in length, with a weight of 18 g and a displacement volume of 5 ml. The pump rotor contains the permanent magnet of a brushless direct current motor and mounts the impeller blades. A titanium shell accommodates the rotor and suspends it at each end by tiny, blood-immersed ceramic bearings. The adult pump functions at speeds of 8,000–12,000 rpm, achieving blood flow up to 8 L/min. The pediatric version of the Jarvik 2000 achieves pump flows of up to 3 L/min. Noise and hemolysis are minimal with each device. Percutaneous power is delivered from external batteries via a controller unit. Internal electrical wires are brought via the left pleural cavity to the apex of the chest and then subcutaneously across the neck to the base of the skull, where a percutaneous titanium pedestal transmits fine electrical wires through the skin of the scalp. The Jarvik 2000 LVAD is currently in human trials.

7.5.7.3. DeBakey LVAD

The DeBakey LVAD is an axial flow pump that measures ~86 mm long and 25 mm wide (about the size of an AA battery)[66–70] (Figure 7.16). It weighs 95 g and has a displacement of 15 cm^3. Within the flow tube, the components consist of an inducer-impeller (the only moving part), a fixed flow straightener that acts as the front-bearing support for the inducer-impeller, and a fixed rear diffuser that provides the rear bearing of the inducer-impeller. The diffuser retards the highly tangential blood flow velocity by redirecting it axially, an action that results in fluid pressure build. Rare earth magnets, which are embedded in the blades of the impeller, act as the rotor of the brushless motor, causing it to spin in a magnetic field. The pump is designed to produce flows of 5 L/min against 100-mmHg pressure with a rotor speed of 10,000 rpm with less than 10 W of power. Extensive computational fluid dynamics analyses were performed jointly with NASA-Ames Research Center to optimize the hydraulic performance and minimize hemolysis of the pump. The DeBakey LVAD is currently under investigation in human trials.

7.6. Total Artificial Hearts

7.6.1. CardioWest C-70 Total Artificial Heart

The CardioWest C-70 total artificial heart (SynCardia Systems, Inc., Tucson, AZ) is a pulsatile biventricular cardiac replacement system recently approved by the FDA as a bridge to heart transplantation[71–74] (Figure 7.17). The rigid polyurethane pump contains a smooth, flexible polyurethane diaphragm that separates the blood and air chambers. Two Medtronic-Hall mechanical valves located at the inflow and outflow orifices provide unidirectional blood flow. Compressed air from the external drive console moves the diaphragm upward causing ejection of blood. The pump has a maximum stroke volume of 70 ml and a maximum flow rate of 15 L/min, although the average flow rate is <8 L/min. Pump rate, duration of systole, and driving pressure can be adjusted to achieve optimal flow conditions. The total artificial heart is surgically implanted in the mediastinal space after the ventricles have been excised, while the atrial cuffs are retained. The pneumatic drivelines are externalized percutaneously and attached to the drive console. Anticoagulation with dipyridamole, heparin, and warfarin is necessary to prevent thrombus formation. Patients may be ambulatory, but their mobility is frequently restricted by the large drive console. In a recent study, Copeland and colleagues reported a 79% survival to heart transplantation compared to 46% for the observational arm. One-year posttransplant survival was 86%.

DropBooks

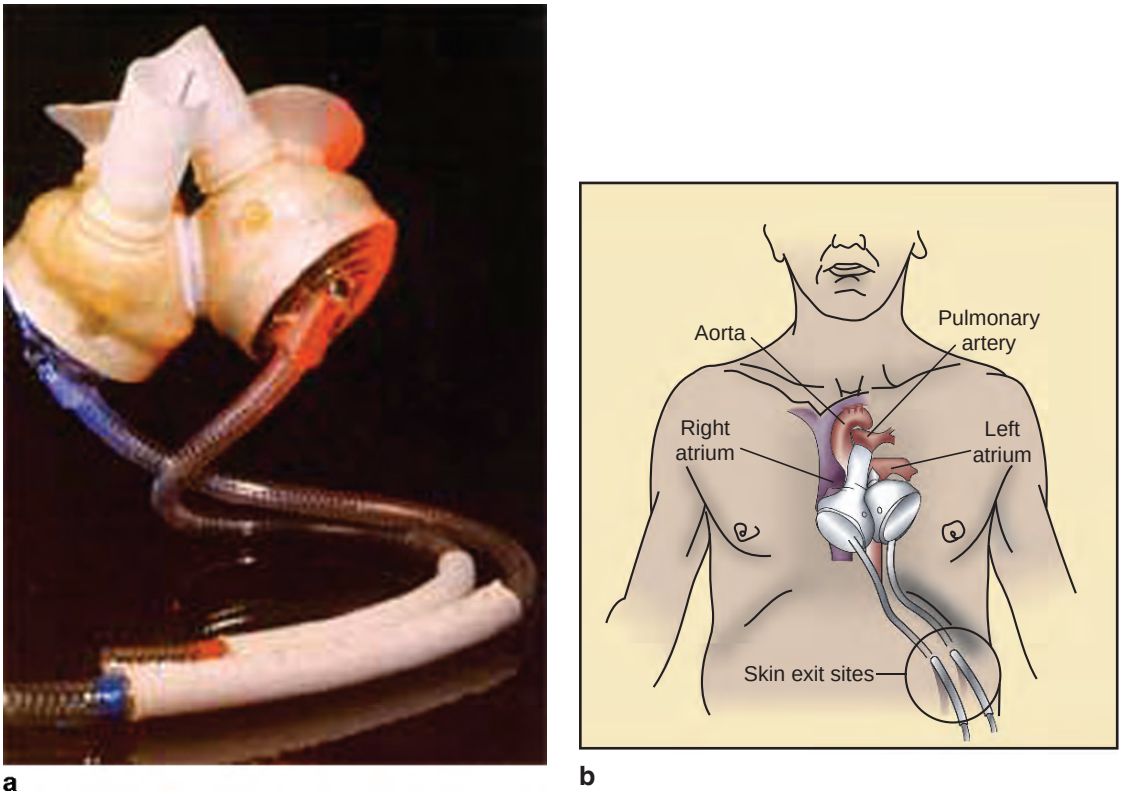


FIGURE 7.17. **A** CardioWest 70 Total Artificial Heart. B Schematic representation of the orthotropic placement of the total artificial heart.

7.7. Summary

There are currently several safe and effective options to provide temporary circulatory support for patients presenting with cardiogenic shock or refractory heart failure. Newer device designs are currently being developed that will increase the options available to our patients. Because of the technological advancements, it will be difficult to predict what devices will ultimately prove to be the most efficacious. It is likely that a variety of devices will be necessary, depending on clinical circumstances and patient characteristics. Using ECMO or ECLS as an initial bridge or screen before longer support is instituted works well. Bridging to recovery is relatively uncommon, compared to bridging to transplantation.

Key points to Remember

- Mechanical circulatory support of critically ill patients is highly effective and reasonably safe in the setting of cardiogenic shock or refractory heart failure.
- Bridging with mechanical devices to recovery of cardiac function is relatively uncommon, but may occur in select circumstances.
- ECMO or ECLS may act as a good screen of temporary support before deciding if patients are suitable for longer term support.
- Recent improvements in technology have resulted in a wide array of exciting devices that show great promise in terms of efficacy and longevity in mechanical support of the failing heart.

References

1. Hochman JS, Sleeper LA, Webb JG, et al. Early revascularization in acute myocardial infarction complicated by cardiogenic shock. *NEJM*. 1999;341:625-634.
2. Khot UN, Mishra M, Smedira NG, et al. Acute renal failure complicating cardiogenic shock is not a contraindication to mechanical support as a bridge to cardiac transplantation. *Circulation*. 2001;104(suppl II):II-714 (abstract).
3. Deng MC, Loebe M, El-Banayosy A, et al. Mechanical circulatory support for advanced heart failure: Effect of patient selection on outcome. *Circulation*. 2001;103:231-237.
4. Frazier OH, Rose EA, Oz MC, et al. Multicenter clinical evaluation of the HeartMate vented electric left ventricular assist system in patients awaiting heart transplantation. *J Thorac Cardiovasc Surg*. 2001;122:1186-1195.
5. El-Banayosy A, Arusoglu L, Kizner L, et al. Predictors of survival in patients bridged to transplantation with the Thoratec VAD device: A single center retrospective study on more than 100 patients. *J Heart Lung Transplant*. 2000;19:964-968.
6. Pae WE. Ventricular assist devices and total artificial hearts: A ASAIO-ISHLT Registry experience. *Ann Thorac Surg*. 1993;55:295-298.
7. Guyton RA, Schonberger J, Everts P, et al. Postcardiotomy shock: Clinical evaluation of the BVS 5000 biventricular support system. *Ann Thorac Surg*. 1993;56:346-356.
8. Jett GK. Postcardiotomy support with ventricular assist devices: Selection of recipients. *Semin Thorac Cardiovasc Surg*. 1994;6:136-139.
9. Samuels LE, Kaufman MS, Thomas MP, et al. Pharmacologic criteria for ventricular assist device insertion following postcardiotomy shock: Experience with the Abiomed BVS system. *J Card Surg*. 1999;14:288-293.
10. Farrar DJ, Hill JD, Pennington DG, et al. Preoperative and postoperative comparison of patients with univentricular and biventricular support with the Thoratec ventricular assist device as a bridge to cardiac transplantation. *J Thorac Cardiovasc Surg*. 1997;113:202-209.
11. Kormos RL, Gasior TA, Kawai A, et al. Transplant candidate's clinical status rather than right ventricular function defines the need for univentricular versus biventricular support. *J Thorac Cardiovasc Surg*. 1996;111:773-783.
12. Rao V, Slater JP, Edwards NM, Naka Y, Oz MC. Surgical management of valvular disease in patients requiring left ventricular assist device support. *Ann Thorac Surg*. 2001;71:1448-1453.
13. Rose AG, Park SJ, Bank AJ, Miller LW. Partial aortic valve fusion induced by left ventricular assist device. *Ann Thorac Surg*. 2000;70:1270-1274.
14. Moazami N, Argenziano M, Kohmoto T, et al. Inflow valve regurgitation during left ventricular assist device support may interfere with reverse ventricular remodeling. *Ann Thorac Surg*. 1998;65:628-631.
15. Santamore WP, Gray LA. Left ventricular contributions to right ventricular systolic function during LVAD support. *Ann Thorac Surg*. 1996;61:350-356.
16. Pavie A, Leger P. Physiology of univentricular versus biventricular support. *Ann Thorac Surg*. 1996;61:347-349.
17. Mandarino WA, Winowich S, Gorcsan J, et al. Right ventricular performance and left ventricular assist device filling. *Ann Thorac Surg*. 1997;63:1044-1049.
18. Shapiro GC, Leibowitz DW, Oz MC, et al. Diagnosis of patent foramen ovale with transesophageal echocardiography in a patient supported with a left ventricular assist device. *J Heart Lung Transplant*. 1995;14:594-597.
19. Goldstein DJ, Seldomridge JA, Chen JM, et al. Use of aprotinin in LVAD recipients reduces blood loss, blood use, and perioperative mortality. *Ann Thorac Surg*. 1995;59:1063-1068.
20. Kaplon RJ, Gillinov AM, Smedira NG, et al. Vitamin K reduces bleeding in left ventricular assist device recipients. *J Heart Lung Transplant*. 1999;18:346-350.
21. Oz MC, Goldstein DJ, Pepino P, et al. Screening scale predicts patients successfully receiving long-term implantable left ventricular assist devices. *Circulation*. 1995;92(suppl II):II-169-II-173.
22. Ochiai Y, McCarthy PM, Smedira NG, et al. Implantable left ventricular assist device insertion: Analysis of 245 patients. *Circulation*. 2002;106(suppl I):I-198-I-202.
23. Nakatani S, Thomas JD, Savage RM, et al. Prediction of right ventricular dysfunction after left ventricular assist device implantation. *Circulation*. 1996;94(9, suppl):II-216-II-221.
24. Argenziano M, Choudhri AF, Moazami N, et al. Randomized, double-blind trial of inhaled nitric oxide in LVAD recipients with pulmonary hypertension. *Ann Thorac Surg*. 1998;65:340-345.
25. Argenziano M, Catanese KA, Moazami N, et al. The influence of infection on survival and successful transplantation in patients with left ventricular assist devices. *J Heart Lung Transplant*. 1997;16:822-831.
26. Holman EL, Murrah CP, Ferguson ER, et al. Infections during extended circulatory support: University of Alabama at Birmingham experience 1989 to 1994. *Ann Thorac Surg*. 1996;61:366-371.
27. Moulopoulos SD, Topaz S, Kolff WJ. Diastolic balloon pumping (with carbon dioxide) in the aorta:

DropBooks

A mechanical assistance to the failing circulation. *Am Heart J*. 1962;63:669.
28. Kantrowitz A, Tjonneland S, Freed PS, et al. Initial clinical experience with intraaortic balloon pumping in cardiogenic shock. *JAMA*. 1968;203:135.
29. Claus RH, Birtwell WC, Albertal G, et al. Assisted circulation, the arterial counterpulsator. *J Thorac Cardiovasc Surg*. 1961;41:447.
30. Ferguson JJ III, Cohn M, Freedman Jr RJ, et al. The current practice from the benchmark registry. *J Am Coll Cardiol*. 2001;38:1456-1462.
31. Muehrcke DD, McCarthy PM Stewart RW, et al. Extracorporeal membrane oxygenation for post-cardiotomy cardiogenic shock. *Ann Thorac Surg*. 1996;61:684-691.
32. Smedira NG, Wudel JH, Hlozek CC, et al. Venovenous extracorporeal life support for patients after cardiotomy. *ASAIO J*. 1997;43:M444-M446.
33. McGovern GJ, Magovern JA, Benckart DH, et al. Extracorporeal membrane oxygenation-preliminary results in patients with postcardiotomy cardiogenic shock. *Ann Thorac Surg*. 1994;57:1462-1467.
34. Bartlett RH, Roloff DW, Custer JR, et al. Extracorporeal life support: The University of Michigan experience. *JAMA*. 2000;283:904-908.
35. Hill JD, O'Brien TG, Murray JJ, et al. Extracorporeal oxygenation for acute post-traumatic respiratory failure. *N Engl J Med*. 1972;286:629-634.
36. Pagani FD, Lynch W, Swaniker F, et al. Extracorporeal life support to left ventricular assist device bridge to heart transplant: A strategy to optimize survival and resource utilization. *Circulation*. 1999;100(19):II206-II210.
37. Pagani FD, Aaronson KD, Dyke DB, Wright S, Swaniker F, Bartlett RH. Assessment of an extracorporeal life support to LVAD bridge to heart transplant strategy. *Ann Thorac Surg*. 2000;70:1977-1985.
38. Bowen FW, Carboni AF, O'Hara ML, et al. Application of "double bridge mechanical" resuscitation for profound cardiogenic shock leading to cardiac transplantation. *Ann Thorac Surg*. 2001;72:86-90.
39. Smedira NG, Moazomi N, Golding CM, et al. Clinical experience with 202 adults receiving extracorporeal membrane oxygenation for cardiac failure: Survival at five years. *J Thorac Cardiovasc Surg*. 2001;122:92-102.
40. Magovern GJ, Simpson KA. Extracorporeal membrane oxygenation for adult cardiac support: The Allegheny experience. *Ann Thorac Surg*. 1999;68:655-661.
41. Thiele H, Lauer B, Hambrecht R, Boudriot E, Cohen HA, Schuler G. Reversal of cardiogenic shock by percutaneous left atrial-to-femoral arterial bypass assistance. *Circulation*. 2001;104:2917-2922.
42. Siegenthaler MP, Brehm K, Strecker T, et al. The Impella Recover microaxial left ventricular assist device reduces mortality for postcardiotomy failure: A three-center experience. *J Thorac Cardiovasc Surg*. 2004;127:812-822.
43. Meyns B, Dens J, Sergeant P, Herijgers P, Daenen W, Flameng W. Initial experiences with the Impella device in patients with cardiogenic shock—Impella support for cardiogenic shock. *Thorac Cardiovasc Surg*. 2003;51(6):312-317.
44. McBride LR, Naunheim KS, Fiore AC, et al. Clinical experience with 111 Thoractec ventricular assist devices. *Ann Thorac Surg*. 1999;67:1233-1238.
45. El-Banayosy A, Korfer R, Arusoglu L, et al. Bridging to cardiac transplantation with the Thoratec ventricular assist device. *Thorac Cardiovasc Surg*. 1999;47(suppl 2):307-310.
46. Farrar DJ, Buck KE, Coulter JH, et al. Portable pneumatic biventricular driver for the Thoratec ventricular assist device. *ASAIO J*. 1997;43:M631-M634.
47. Gray LA, Champsaur GG. The BVS 5000 biventricular assist device. The worldwide registry experience. *ASAIO J*. 1994;40:M460-M464.
48. Samuels LE, Holmes EC, Thomas MP, et al. Management of acute cardiac failure with mechanical assist: Experience with the Abiomed BVS 5000. *Ann Thorac Surg*. 2001;71:S67-S72.
49. Pagani FD, Aaronson KD. Mechanical circulatory support. In: Greenfield LJ, Editor-In-Chief. *Surgery: Scientific Principles and Practice*. 3rd ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.
50. Frazier OH, Myers TJ, Radovancevic B. The HeartMate left ventricular assist systems—Overview and 12 year experience. *Tex Heart Inst J*. 1998;25:265-271.
51. McCarthy PM, Smedira NO, Vargo RL, et al. One hundred patients with the HeartMate left ventricular assist device: Evolving concepts and technology. *J Thorac Cardiovasc Surg*. 1998;115:904-912.
52. Frazier OH, Rose EA, Oz MC, et al. Multicenter clinical evaluation of the HeartMate vented electric left ventricular assist system in patients awaiting heart transplantation. *J Thorac Cardiovasc Surg*. 2001;122:1186-1195.
53. Morgan JA, John R, Rao V, et al. Bridging to transplant with the HeartMate left ventricular assist device: The Columbia Presbyterian 12-year experience. *J Thorac Cardiovasc Surg*. 2004;127:1309-1316.
54. Long JW. Advanced mechanical circulatory support with the HeartMate left ventricular assist device in the year 2000. *Ann Thorac Surg*. 2001;71:176-182.
55. Robbins RC, Oyer PE. Bridge to transplant with the Novacor left ventricular assist system. *Ann Thorac Surg*. 1999;68:695-697.
56. El-Banayosy A, Deng M, Loisance DY, et al. The European experience of Novacor left ventricular assist (LVAS) therapy as a bridge to transplant: A retrospective multi-centre study. *Eur J Cardiothorac Surg*. 1999;15:835-841.

57. Murali S. Mechanical circulatory support with the Novacor LVAS: World-wide clinical results. *Thorac Cardiovasc Surg*. 1999;47(suppl 2):321-325.
58. Reichenbach SH, Farrar DJ, Hill JD. A versatile intracorporeal ventricular assist device based on the thoratec VAD system. *Ann Thorac Surg*. 2001;71: S171-S175.
59. Thomas DC, Butler KC, Taylor LP, et al. Progress on development of the Nimbus-University of Pittsburgh axial flow left ventricular assist system. *ASAIO J*. 1998;44:M521-M524.
60. Butler KC, Dow JJ, Litwak P, et al. Development of the Nimbus/University of Pittsburgh Innovative Ventricular Assist System. *Ann Thorac Surg*. 1999;68:790-794.
61. Griffith BP, Kormos RL, Borovetz HS, et al. HeartMate II left ventricular assist system: From concept to first clinical use. *Ann Thorac Surg*. 2001;71:116-120.
62. Westaby S, Katsumata T, Evans R, et al. The Jarvik 2000 Oxford System: Increasing the scope of mechanical circulatory support. *J Thorac Cardiovasc Surg*. 1997;114:467-474.
63. Westaby S, Katsumata T, Houel R, et al. Jarvik 2000 Heart: Potential for bridge to myocyte recovery. *Circulation*. 1998;98:1568-1574.
64. Frazier OH, Myers TJ, Gregoric ID, et al. Initial clinical experience with the Jarvik 2000 implantable axial-flow left ventricular assist system. *Circulation*. 2002;105:2855-2860.
65. Westaby S, Frazier OH, Beyersdorf F, et al. The Jarvik 2000 Heart. Clinical validation of the intraventricular position. *Eur J Cardiothorac Surg*. 2002;22:228-232.
66. Frazier OH, Myers TJ, Westaby S, Gregoric ID. Clinical experience with an implantable, intracardiac, continuous flow circulatory support device: Physiologic implications and their relationship to patient selection. *Ann Thorac Surg*. 2004;77:133-142.
67. Salzberg S, Lachat M, Zünd G, et al. Left ventricular assist device as bridge to heart transplantation—Lessons learned with the MicroMed DeBakey axial blood flow pump. *Eur J Cardiothorac Surg*. 2003;24:113-118.
68. DeBakey ME. Development of a ventricular assist device. *Artif Organs*. 1997;21:1149-1153.
69. DeBakey ME. A miniature implantable axial flow ventricular assist device. *Ann Thorac Surg*. 1999;68:637-640.
70. Fossum TW, Morley D, Benkowski R, et al. Chronic survival of calves implanted with the DeBakey ventricular assist device. *Artif Organs*. 1999;23:802-806.
71. Wieselthaler GM, Schima H, Hiesmayr M, et al. First clinical experience with the DeBakey VAD continuous-axial-flow pump for bridge to transplantation. *Circulation*. 2000;101:356-359.
72. Arabia FA, Copeland JG, Pavie A, et al. Implantation technique for the CardioWest total artificial heart. *Ann Thorac Surg*. 1999;8:698-704.
73. Copeland JG, Smith RG, Arabia FA, et al. Cardiac replacement with a total artificial heart as a bridge to transplantation. *N Engl J Med*. 2004;351:859-867.
74. Copeland JG, Smith RG, Arabia FA, et al. Total artificial heart bridge to transplantation: A 9-year experience with 62 patients. *J Heart Lung Transplant*. 2004;23:823-831.
75. Copeland JG, Arabia FA, Tsau PH, et al. Total artificial hearts: Bridge to transplantation. *Cardiol Clin*. 2003;21:101-113.

DropBooks

8
Left Ventricular Reconstruction in Ischemic Cardiomyopathy

Salim Aziz, Constantine Athanasuleas, and Jai Raman

8.1. Introduction

Repair of left ventricular aneurysms was reported as early as the late 1950s by Likoff and Bailey (1). Cooley reported on the success of linear closure of these aneurysms (2).

Josephson and Harken described blind endocardial resection for VT with poor functional results (3). Gorlin was among the first to show that the ventricular wall after myocardial infarct could be akinetic or dyskinetic (4). Dor and co-workers described a technique (5) which is illustrated in Figure 8.1 to close the left ventricle reorganizing a neo left ventricular apex, in an attempt to recreate the normal conical shape in 1985. Jatene also described a plication technique in the same year using an external circular set of sutures (6). However, it was Batista's bold experiments in dilated cardiomyopathy with heart failure and very public presentations of his "successes" that made people in the heart failure arena consider left ventricular reconstruction seriously (7).

Despite all this intuitive work on preserving left ventricular geometry, there was little interest in adopting these techniques into widespread clinical practice.

The 1980s were marked by two important steps in the knowledge of evolution and prevalence of ischemic failing ventricles:

1. The mechanism of progressive ventricular dilatation following transmural myocardial infarction, also known as remodelling, was well analysed and characterized (8). The role of neurohormonal activation was established and this helped to provide therapeutic targets (9). Ischemic remodelling leads to progressive ventricular dilatation which then sets in motion the cascade of heart failure (10).
2. Aggressive treatment of acute myocardial infarction, by revascularization of the occluded artery, has resulted in improved the survival rates. However, even after successful re-canalization, the left ventricular wall of survivors, remains affected by scar in 80–100% of cases; the infarct size varying from 6 to 60% of the ventricular surface area as indicated by Christian et al. (11).

Various imaging modalities such as cardiac magnetic resonance (CMR) developed as accurate, reliable and reproducible tools (12) to assess both anatomy and performance of the ventricles after infarction. Use of contrast MRI further enhanced the utility of this imaging modality (13).

More recently, three-dimensional echocardiography and volume rendered images with multi-detector CT scanning have shown particular promise in this arena.

8.2. Fate of the Left Ventricle After Infarction

Gorlin in 1967 observed that: "when 20% to 25% of LV area is asynergic, contraction of the myofibers to maintain stroke volume exceeds pathophysiological limits and cardiac enlargement (by the Frank-Starling mechanism) must ensue to maintain cardiac output".

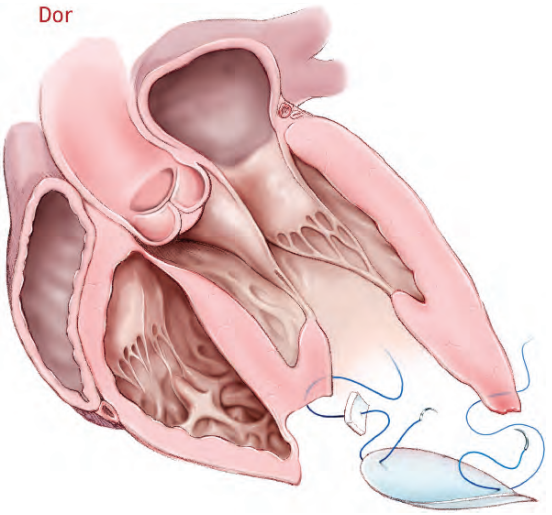


FIGURE 8.1 Schematic of the principles of left ventricular reconstruction (as proposed by Dor in 1985)

"There are two types of asynergy seen as consequence of ventricular aneurysms: regional akinesis (total lack of wall motion), and regional dyskinesis (paradoxical systolic expansive wall motion".

In spite of revascularization of the culprit artery altering the immediate prognosis, the left ventricular wall may remain diseased (14).

8.2.1. Evolution of the Infarcted Area

The infarcted wall undergoes changes that start with necrosis, progress to fibrosis and, eventually to calcification

1. The typical left ventricular aneurysm is characterized by a transmural infarct (Figure 8.2).
2. The use of thrombolysis and/or revascularization in the acute phase may prevent transmural necrosis (Figure 8.2b). Ventricular muscle adjacent to the epicardial artery is salvaged by re-canalization, but the subendocardial muscle is necrotic, as described by Bogaert in 1997 (14). The resultant ventricular wall may have viable myocardium which maybe evident at surgery (or during Thallium test) surrounding an akinetic, necrotic zone. The scarred asynergic ventricular wall may result in dyskinesia or akinesia. In both morphologies, it is important to know the extent of ventricular wall that is abnormal, since this determines the indications and prognosis of surgical intervention.
3. *Location*: The *antero-apical and septal* regions are most commonly involved in anterior infarctions caused by left anterior descending artery occlusion. Involvement of the septum is difficult to assess on ventriculography. The septum is best assessed by biplane angiography, echocardiography or cardiac MRI.

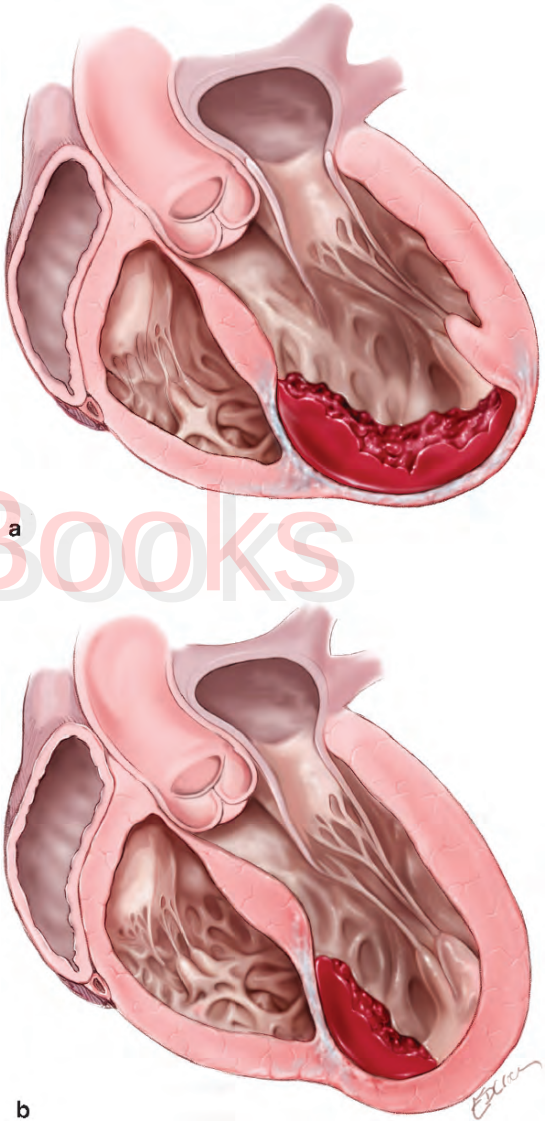


FIGURE 8.2 Anteroseptal infarcts with extensive apical and septal involvement (**a**), Anterior infarct with predominantly septal involvement (**b**). Note adjacent mural thrombus formation

DropBooks

4. The extent of asynery or abnormality governs the prognosis of the left ventricle after infarction. This can be assessed by a variety of imaging techniques. Traditionally angiography using the centerline method in the right oblique projection has been used. However, increasingly, other techniques such as contrast echocardiography, radionuclide ventriculography, multi-slice CT Scan, cardiac magnetic resonance (MRI), provide more information. Analysing the LV wall and the presence of a necrotic scar is very important. The extent of asynergy can be expressed as the ratio between the length of necrotic wall and the total length of the LV circumference. The progression towards severe heart failure is likely when this ratio reaches 50%.

8.2.2. Fate of the Non-Infarcted Myocardium

While normal at first, the undamaged myocardium undergoes hypertrophy to compensate for the lack of contractility of the necrotic wall, and finally dilates by a combination of mechanical forces and neurohormonal signalling. The Frank-Starling mechanism explains the early dilatation that temporarily improves the cardiac output and function. Laplace's Law described increased wall stress and this is the fundamental reason behind the deleterious effects on myocardial contractility due to increased wall tension. Left ventricular remodelling is the term used to describe the progressive dilatation of the heart, and is based on a set of complex inflammatory and neurohormonal processes. Gaudron suggested that the culmination of this process is progressive dilatation of the non-infarcted area with an ensuing spherical shape and akinesia, which occurs, in 20% of patients treated for myocardial infarction (15).

Harvey White was an early proponent of using left ventricular volume as a sensitive marker of post-infarction ventricular dysfunction (16). Yamaguchi used left ventricular end-systolic volume as an important predictor for prognosis after surgical repair (17). Doubling of indices can be considered markers of severe dilatation (normal values are 25–30 ml/m^2 for end-systolic volume index (ESVI) and 50/60 ml/m^2 for end-diastolic volume index (EDVI).

8.3. Who Should be Considered for Surgical Ventricular Restoration (SVR) or Left Ventricular Reconstruction (LVR)?

Currently SVR is largely established for patients with ischemic cardiomyopathy after myocardial infarction, although some have advocated a variant of the technique for patients with idiopathic dilated cardiomyopathy.

Presently the "ideal" patient should have a dilated ventricle and NYHA class III to IV heart failure symptoms following infarction. As for patients with LV aneurysms, totally asymptomatic patients should not be considered. The SVR/LVR is advocated for patients with a prior left anterior descending artery territory infarct (anterior wall, septum region). Patients with both LAD and circumflex artery occlusions may not be suitable candidates. The infarcted segment can either be akinetic or dyskinetic.

The timing of surgery is also important. Conventional wisdom states that six weeks following infarction should elapse before SVR is considered. There is, however, one small series of seven patients that underwent surgery soon after a large anterior infarction with encouraging results (18). Anecdoctal cases have been performed in the early post-infaction period (2–14 days), particularly in the setting of low cardiac output as salvage therapy.

8.4. Preparation for Surgery

1. *Pre-operative preparation*: Patients that have been inpatients in cardiology for recurrent episodes of CHF and titration of medical therapy, often need tuning up. A variety of tests may be of benefit:

(a) Measurement of pulmonary arterial pressure (PAP) by right heart catheterisation and the response to vasodilator therapy, and/or oxygen administration helps in stratifying patients.
(b) Detailed echocardiographic assessment including three-dimensional echocardiography is of great benefit. Mitral regurgitation has to be assessed by pre-operative echocardiography or trans-esophageal echocardiography if necessary.

(c) The extent of the scar and its location are important in planning the operation. Establishing viability of the remote non-infarcted segments is crucial because often there are regional wall motion abnormalities in these areas. Gadolinium enhanced magnetic resonance imaging is a good test of viability. Segments that are hypokinetic predictably improve if there is no hyperenhancement. If MRA is contraindicated due to implantation of a defibrillator or pacemaker, multi slice CT scan or 3-D echocardiography may be used. However, these tests may only assess contractility of the remote segments.
(d) A coronary angiogram is mandatory to delineate the coronary anatomy.

2. *Pre-operative medical treatment is continued* except for cessation of anti-platelet and anti-coagulant therapy. The intra-aortic balloon pump (IABP) should be used whenever there is hemodynamic compromise, such as evolving infarction without remission, CHF not improved by medical therapy, patients with a mechanical complication of myocardial infarction, or incipient renal failure. Some have found it useful in all SVR procedures as adjuvant therapy.
3. *Specific operative procedures*: A femoral arterial line is inserted for monitoring purposes and to allow quick access for insertion of a balloon pump if required. The patient is prepared for saphenous vein harvest if required. Cannulation for cardiopulmonary bypass is routine, utilizing an aortic cannula and a dual stage right atrial cannula. Monitoring includes arterial line, central venous pressure and Swan Ganz catheter. Transesophageal echocardiography is used routinely.

For the management of cardiopulmonary bypass, we minimize crystalloid use. Retrograde autologous priming of the circuit helps remove the crystalloid that is added to prime the circuit. Hemofiltration during bypass in helpful in reducing myocardial oedema.

8.4.1. Left Ventricular Reconstruction (LVR)

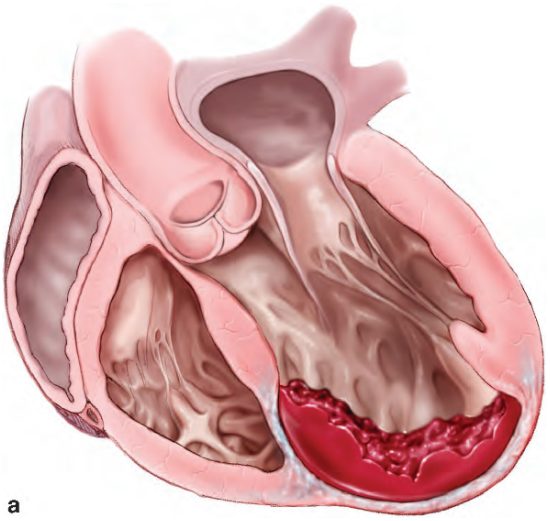
Sequence of surgical steps may depend on the acuity of the patient, the extent of ischemia, presence or absence of left ventricular thrombus, etc. (Figure 8.3).

1. The repair may be conducted utilizing the open-beating or cardioplegic arrest methods of myocardial protection.

Figure 8.4 shows implant of an endoventricular patch.

2. Grafting all coronary arteries with meticulous myocardial protective strategies is important.

DropBooks



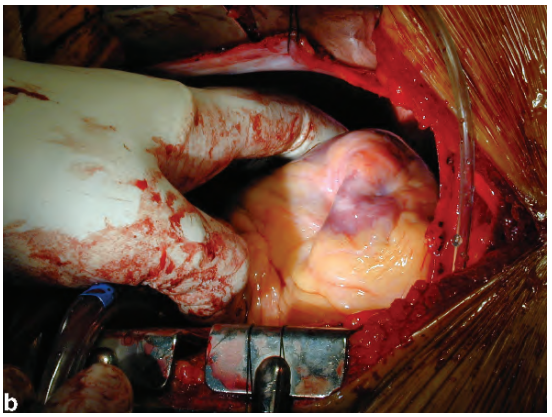
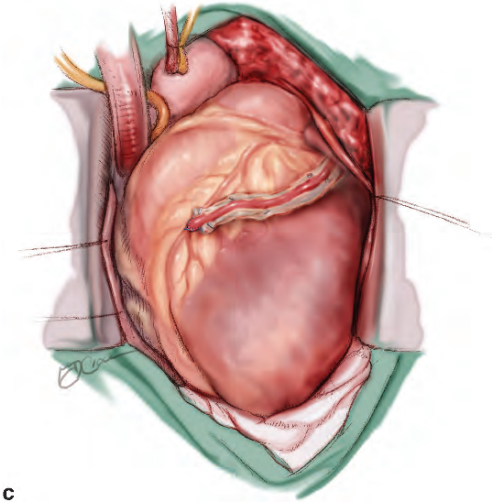
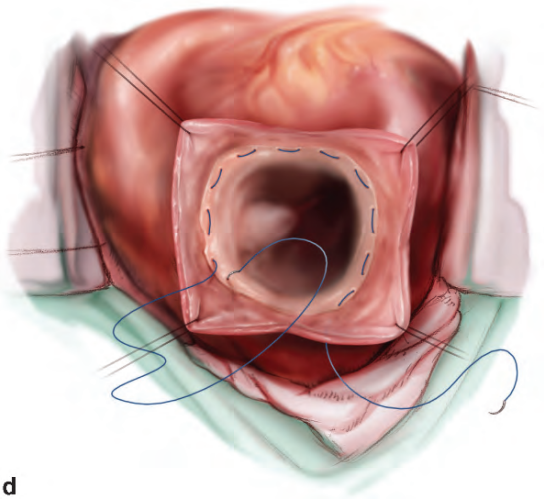


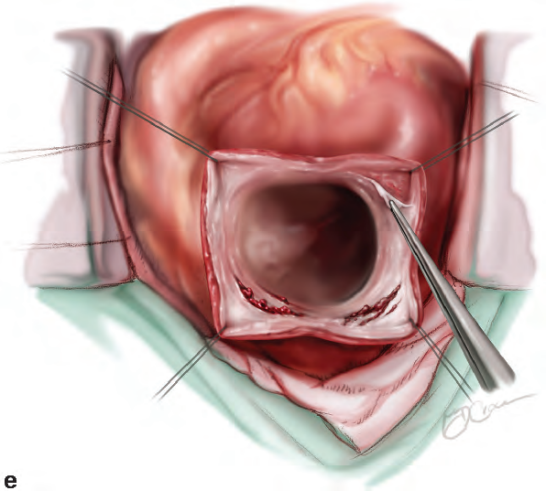
FIGURE 8.3 Steps of surgery for left ventricular reconstruction (LVR) **a** The antero septo apical aneurysm with mural thrombi: the dilatation also affects the non-scarred myocardium on septum (S) and lateral wall (L). **b** Intra-operative photograph showing dimpling of Left ventricular scar with use of vent. **c** Coronary revascularization accomplished first on arrested heart.



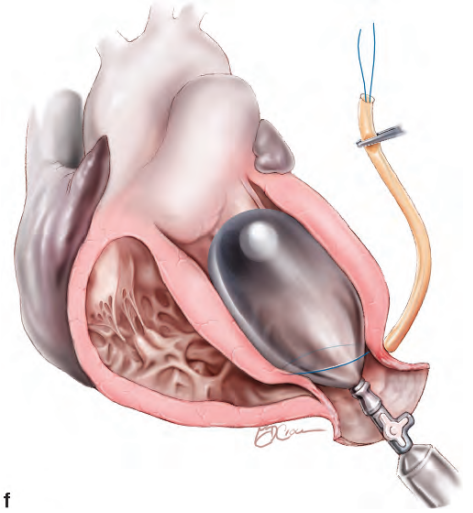
c



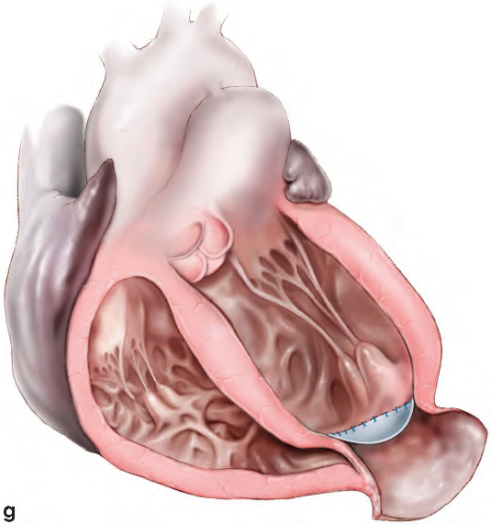
d



e



f



g

FIGURE 8.3 (continued) **d** The continuous purse-string suture at the limit between fibrous and normal myocardium (Fontan "Trick"). **e** Possible endocardectomy if needed. **f** The suture is tied on a rubber balloon inflated to 50 mm per square meter of the body surface area (normal diastolic volume). The shortening of the SL length illustrates the reorganization of the curvature. **g** The Dacron patch anchored on the suture. The right ventricle apex projects beyond the new LV apex

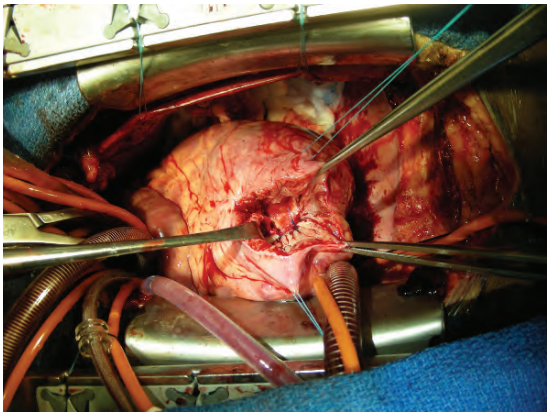


FIGURE 8.4 Completed patch implant

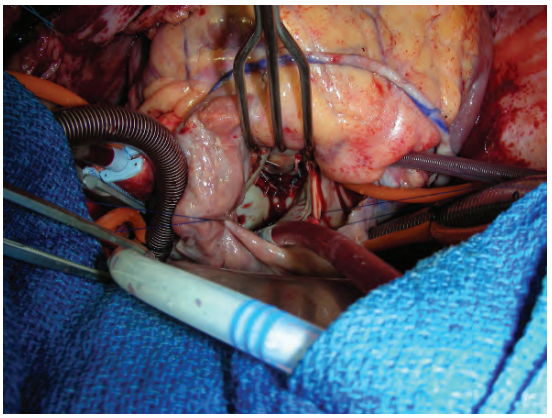


FIGURE 8.5 Completed mitral valve repair. Note vein graft to inferior to a branch of the RCA and trans-septal approach to mitral valve

Retrograde cardioplegia preserves septal contractility as is crucial in preventing low output states post-operatively. Particular care is taken to revascularize the LAD, or diagonal if possible, thereby increasing septal blood flow.

What is the best resultant shape/volume of the operated left ventricle? What sort of patch should be used? These are interesting questions that are yet to be resolved conclusively. Although some authors have suggested that the LV can be "tailored" without a patch, this can be difficult, especially for the novice surgeon. This technique promoted by McCarthy is described in the next chapter. The size of the patch and the stiffness of the patch also may have a bearing on the outcome long-term, and these matters are addressed in the next chapter.

Management of Associated Mitral Regurgitation: Mitral regurgitation is found often in these patients, either due to the nature of the remodelling or due to involvement of the infero-basal wall of the left ventricle. Our personal preference to correct any degree of mitral regurgitation that is greater than moderate or 2+. Typically, this is done by utilizing a flexible posterior band or a remodelling annuloplasty ring. At times a simple Alferi stitch maybe resorted to as well. The mitral valve can be accessed and repaired through the ventriculotomy or via a separate incision in the left atrium or a trans-septal approach. The limitation of the ventricular approach is that access to the valve may be suitable only in very large scars that are more apico-septal in orientation.

Figure 8.5 shows a completed mitral valve repair in a patient undergoing left ventricular reconstruction.

1. *The LVR technique*: Dor reported the technique of endoventricular patch patch plasty in 1989 (19). In this classic technique, the ventricular wall is opened at the centre of the scarred area, which often appears as a dimpled area once a left ventricular vent is placed after aortic cross clamping (Figure 8.3b). Any clots present are removed. It is important to note that some fragmented and friable small clots may not be seen on trans-esophageal or epicardial echocardiography, especially if the thrombus is non-homogenous or small. The endocardial scar is dissected and re-sected if the scar is calcified (Figure 8.3e) or if there is evidence of ventricular tachycardia (VT). Ablative treatment at the edge of scar usually at the borderzone, with radio-frequency energy or cyoablation is a short adjunctive procedure shown to limit post-operative dysrhythmias.

The reconstruction of the left ventricular cavity is started using a continuous suture 2–0 monofilament purse-string suture (Figure 8.3d) with bites going into the muscle at the borderzone (the junction between the scar and normal myocardium). Typically, this suture is run as a continuous purse-string suture is tightened over a rubber balloon inflated within the cavity at the theoretical diastolic left ventricular volume (50–60 ml/m^2 of BSA). This technique was introduced to avoid making the

DropBooks

residual cavity too small (20). This is a good guide to surgeons with limited experience. The endoventricular circular suture is also known as the "Fontan stitch" (Figure 8.3d) and helps optimize orientation of the patch while selecting its shape and size.

The septum and apex are more involved than the lateral wall in the antero-septo-apical type of scarring. In these cases, the suture, thus placed deeply in the septum, totally excludes the apex and the posterior wall below the base of the posterior papillary muscle, and only a small portion of lateral wall above the base of the antero-lateral papillary muscle. Therefore, the orientation of this new neck (and of the patch) roughly follows the axis of the septum.

Dor described the use of a Dacron patch that is sutured to the Fontan Stitch. The excluded, redundant bits of scar are then sutured over the patch to aide in haemostasis. The traditional Dacron patch is quite stiff, and various modifications of the technique include use of Gortex, bovine pericardium or no patch at all. These are described in subsequent chapters.

2. *Wean off CPB*: Typically, weaning from bypass is slow and gentle to allow complete recovery of both ventricles. Frequent use of antegrade and retrograde blood cardioplegia every 8–10 min helps preserve biventricular function and allows quicker recovery of the heart. Our choice of inotrope typically involves milrinone and dobutamine. Often, norepinephrine and/or vasopressin are required as an adjunct to counter the hypotension that is seen due to the effect of milrinone. Liberal use of the balloon pump has been found to be very useful. Prophylactic atrial and ventricular pacing wires are used to ensure a regular rhythm. If there is a history of atrial fibrillation or ventricular arrhythmia, prophylactic use of amiodarone helps reduce the risk of lethal arrhythmias.
3. *Specific modifications*:

Figure 8.6 shows the left ventricle in longitudinal section with mural thrombus along the septum and antero-apical wall.

(a) Changes based on alterations of the ventricular wall

- Autologous tissue has been used for the patch: either a semicircle of the fibrous endocardial scar mobilized with a septal hinge if this scar is strong, or autologous pericardium.

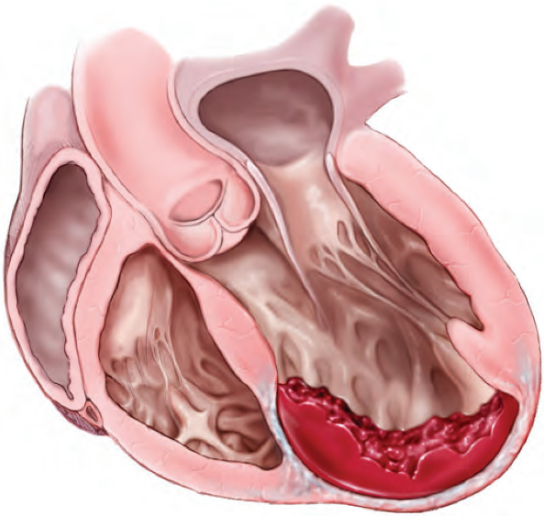


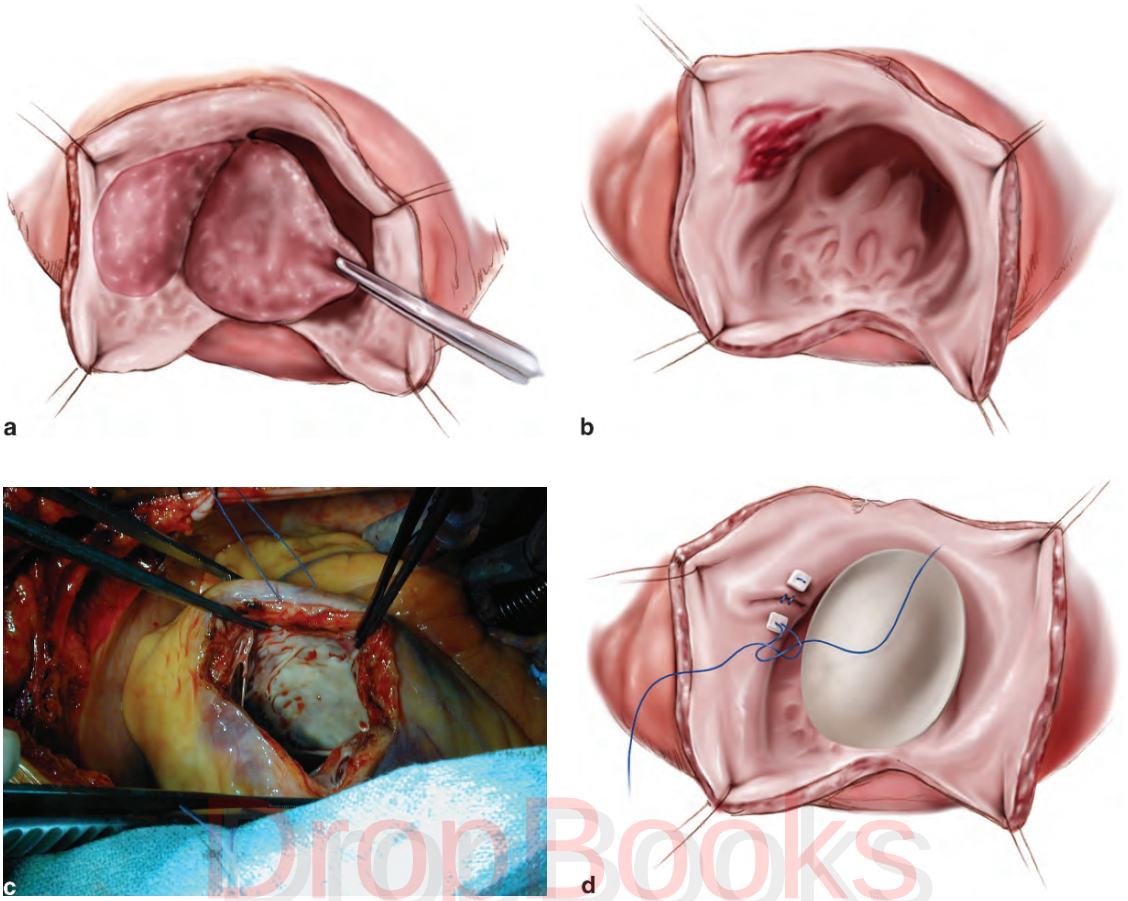
FIGURE 8.6 The left ventricle in longitudinal section with mural thrombus along the septum and antero-apical wall

Figure 8.7a, b show a septal hinge being used to patch the defect.

- When the tissues are soft and necrotic, during the repair of an acute mechanical complication of myocardial infarction (exclusion of septal rupture or treatment of free wall fissures), the patch has to be inserted into healthy tissue by deep stitches reinforced with Teflon pledgets. The patch is anchored above the septal rupture which is excluded from the LV cavity.

Figures 8.7c, d show a septal infarct that has been excluded with a pledgetted plicating suture and subsequent implantation of a patch to exclude the septal infarct.

(b) *Amount of Scar Exclusion*: In cases of a large amount of asynergy (above 50% of LV cavity) surgery is accomplished with some modifications. These patients typically are in Class III or IV heart failure and on inotropes. Mean pulmonary artery pressure is often above 25 mmHg, ejection fraction (EF) below 30%, EDVI above 150 ml/m^2, and ESVI above 60 ml/m^2. Ventricular tachycardia may be present in nearly 50% of cases and this should preferably be addressed by ablative strategies and/or endocardectomy. Mitral insufficiency has to be repaired in the majority of cases. Mitral valve repair in this instance is performed as



DropBooks

FIGURE 8.7 Particular cases of endoventricular patch reconstruction. **a** Utilization of the septal scar as an autologous patch. A semicircular portion of the scar mobilized from the septum with a septal hinge is sutured on contractile muscle inside the left ventricle. **b** Septal Involvement after opening up the left ventricular scar **c** Operative photograph of septal infarct and scar **d** Septal Involvement. The patch is anchored above the septal repair, which is excluded from the left ventricular cavity

a remodelling annuloplasty, with Bolling and his followers advocating rigid, shaped rings. David and his group have shown good results with flexible posterior bands. If the presentation is acute or if there is difficulty in repairing the valve, a valve replacement with chordal preservation should be considered. Theoretically, the exclusion of all scarred areas may lead to a very small LV cavity with a high risk of immediate or delayed diastolic dysfunction. The Fontan stitch is placed slightly beyond the edge of healthy muscle at the transitional area. The use of a mandril or balloon inside the LV, inflated at the theoretical diastolic volume of the patient is a useful guide to optimize tension on the suture. The patch can be slightly more redundant (3 to 4 cm in diameter) than in the usual technique.

If the septum cannot be excluded easily, the redundant septum can be plicated or imbricated separately or at the edge of the patch as described by Jatene.

(c) Inferior and posterior scars: An oblong or triangular patch, with its base aligned along the posterior or postero-lateral mitral annulus and its apex close to the base of the posterior or antero-lateral papillary muscle is the typical orientation. This allows the reconstruction to follow a geometric pattern restoring shape to normal. If the posterior papillary muscle is totally involved in the resected scar, the mitral valve can be replaced by a prosthesis, implanted through the ventriculotomy.

Figure 8.8a–c show repair of a postero-inferior scar with replacement of the mitral valve and implant of a triangular patch.

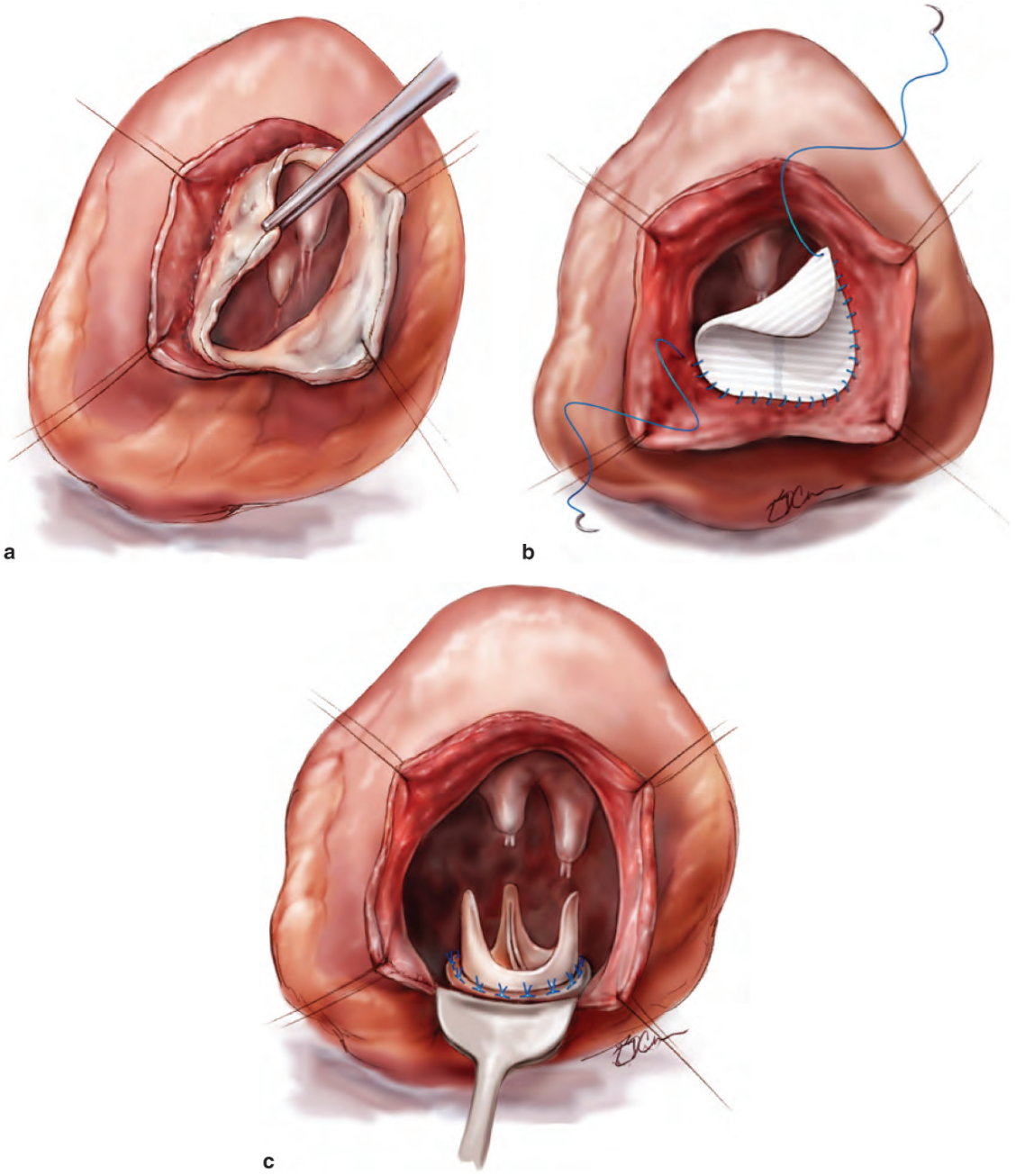


FIGURE 8.8 **a** A: LVR for posterior aneurysm: positioned for posterior incision and endocardectomy **b** Triangular patch closure of the posterior left ventricular scar. **c** Mitral valve replacement through a posterior scar.

8.4.1.1. Early Results

Early results with simple linear closure were variable and often suboptimal.

8.4.1.1.1. Operative Risk and Hospital Mortality

Left ventricular reconstruction is a complex procedure performed on patients with significantly impaired ventricular function and is frequently associated with an operative mortality risk of about 7% (Table 8.1). The risk profile is dependant on the extent of scarring, the degree of heart failure, the amount of remaining normal ventricle, the presence of arrhythmias and the amount of mitral régurgitation. Hospital mortality can be stratified into three categories:

1. Very severely depressed EF < 30%: mortality of 12–15%.
2. EF of 30–40%: mortality of 7%
3. EF > 40%: mortality of 1.3%

8.4.1.1.2. LVR Outcomes (Restore Group)

Dor's contributions inspired a multinational study of ventricular restoration. A collaborative group of cardiologists and cardiac surgeons (the RESTORE Group) from four continents (US, Europe, Asia, South America) applied SVR in 1198 patients between 1998 and 2003 (21). Patients were included in the registry if SVR was performed with the following criteria: prior anterior myocardial infarction, significant ventricular dilation (LVESVI ≥ 60 ml/m^2), and a regional asynergic (non-contractile) area of ≥35%. SVR was most often done as a concomitant procedure: 90% received coronary bypass grafting and mitral valve repair was required in about 20%.

In the RESTORE registry, 86% of patients had NYHA class III/IV symptoms of CHF preoperatively. Such patients have a high mortality with medical therapy, or with surgical revascularization without left ventricular restoration, where late deaths are attributable to CHF. Echocardiography, ventriculography or magnetic resonance angiography (MRA) was used to confirm the asynergic area and calculate the ejection fraction (EF). LVESVI was determined by ventriculography or MRA.

Hospital mortality after SVR was 5.3%, and increased as preoperative ventricular volume rose: 2.3% if LVESVI was <60 ml/m^2, 5.7% if LVESVI was 60–90 ml/m^2, 8.1% if LVESVI was 90–120 ml/m^2 and 8.4% if LVESVI was >120 ml/m^2. These findings are comparable to recently reported mortality rates (5.5–11%) in ischemic patients with left ventricular dysfunction (EF < 35%) undergoing coronary artery bypass grafting alone. The addition of mitral valve repair influenced early outcome. Hospital mortality was 8.7% with mitral repair versus 4.0% without repair ($p < 0.001$). Perioperative mechanical support with intra-aortic balloon pumping was uncommon (< 9%). Global systolic function improved post-operatively as EF increased from 29.6% ± 11.0% preoperatively to 39.5% ± 12.3% post-operatively ($p < 0.001$). LVESVI decreased from 80.4 ± 51.4 ml/m^2 pre-operatively to 56.6 ± 34.3 ml/m^2 post-operatively ($p < 0.001$).

The overall 5-year probability of survival after SVR was 68.6% ± 2.8% and confirms Dor's extensive experience and is unprecedented in the treatment of advanced ischemic cardiomyopathy. The multivariate analysis of SVR demonstrated that major risk factors were age, pre-operative EF, LVESVI, and NYHA functional class.

The RESTORE data further emphasized the importance of measuring LVEVI as a surrogate marker of left ventricular function. EF and LVESVI are not directly related, as there is a wide variation in volume for a given EF. Patients with pre-operative LVESVI ≤ 80 ml/m^2 had long-term survival of 79.4% ± 3.3% as compared to 67.2% ± 3.2% for those with larger hearts. Pre-operative NYHA functional class was also predictive of outcome with decreased 5-year survival in patients with pre-operative class IV symptoms (49.7% ± 5.8% vs 69.9% ± 4.7%

DropBooks

Table 8. 1 Neurohormonal response to LVR in ischemic CM[a]

	EF (%)	EDVI (ml/m^2)	NYHA	NE (pg/ml)	PRA < mμ > g/l/h	A-II (ng/ml)	0BNP (pg/ml)
Pre-operative	23.9	140	2.9	562	5.75	41	771
First Year	36	90	2	319	3.45	23	266

NE norepinephrine, *PA* plasma rennin activity, *A-II* angiotensin II, *BNP* brain natriuretic peptide
[a] Shenk et al. (26)

in class III). These predictors of long-term outcome after SVR are similar to those previously reported. A small number of patients (9%) in functional Class I underwent SVR as an adjunct to CABG because ventricular dilation (LVESVI > 60 ml/m^2) has been shown to be a precursor of late development of CHF and early death.

1. Cardiac morphology and performance:

(a) The most striking findings on imaging are the relative normalcy of ventricular shape and function post-operatively. If a localized scar is effectively excluded with restoration of normal shape, the heart failure symptoms are dramatically ameliorated.
(b) *Improvement in systolic function*: Often, the mean increase in ejection fraction early after reconstruction is between 10 to 20%. Improvement is similar for dyskinetic as well as akinetic lesions (22).
(c) *Improvement in diastolic function***:** The peak filling pressures and filling pressures in the left atrium as surrogate markers of left ventricular diastolic function are relatively normal a few months after operation.
(d) *Efficiency*: The elimination of the dead space of the scar helps improve the efficiency of ventricular contraction by:

- Elimination of the asynergic scar.
- Restoration of the curvature of the ventricular wall: Analysis of pressure-volume curves has shown reduction in wall stress (23).
- Mechanical synchrony is restored.

8.4.1.2. Intermediate and Long-Term Results

1. Despite acceptable early morbidity and mortality, the intermediate and long-term results are not uniform. They are based on a variety of comorbidities and factors. Late mitral regurgitation has been noted to recur in some series (24). We could speculate that this might be related to the stiffness and size of the patch. This may also occur in very large ventricles where there has been a delay of more than 40 months between infarction and surgical repair. Progression in remodelling may depend on mechanical causes or neuro-hormonal activation (25). Continued medical therapy with diuretics, vasodilators, beta-blockers and ACE inhibitors are vital in ensuring good long term outcomes.
2. *Improved left ventricular function and dimensions*: Our experience along with those of others, have shown that there is reverse remodelling of the reconstructed left ventricle over a period of weeks and months. There is a steady improvement in functional status and exercise tolerance in the majority of patients. However, there is a small group of patients where the results may be mediocre, with functional status remaining static or with some deterioration. These are usually patients with diastolic dysfunction or a significant amount of myocardial fibrosis. Occasionally, the underlying cause may be the use of too large a patch or residual mitral regurgitation.

McCarthy reported on the Cleveland Clinic's experience with a variation of the technique whereby the left ventricle was reconstructed without a patch, where they analysed the first data for the first post-operative year (26). These patients had a mean EF 23.9% and mean EDVI 140 ml/m^2, that changed to 36%, and 90 ml/m^2, respectively. The levels of norepinephrine, plasma rennin activity, angiotensin and brain natriuretic peptide decrease significantly, confirming the regression of neurohormonal activation.

3. Long-term results: Global life expectancy at 5 years, in a series of 207 surviving patients analysed from 1991 to 1998, was 82%. In another consecutive series of 245 patients from 1998 to 2003 (analysed to assess the impact of diastolic balloon sizing), the life expectancy at 5 years, hospital death included, is 85% for the global series and 70% for patients with very poor ventricular function (ESVI > 120 ml/m2). At 10 years, in the last category of very largely dilated failing ventricle, the percentage of survivors is 50%, while it is 80% for patients with ESVI < 90 ml/m^2.

8.5. Discussion

8.5.1. Other Surgical Techniques

Beck first described a technique for repair of ventricular aneurysm before the age of the heart-lung machine (27). This early technique utilized a clamp

for resection and repair of aneurysms. Thereafter, the technique evolved to linear closure with use of cardiopulmonary bypass. Eventually, the techniques evolved into a variety of geometric repairs to recreate the conical shape of the left ventricle.

It is difficult to compare linear suture and circular repair, as these techniques can be utilized for the following good indications:

1. A distal anterior and apical bulging true dyskinetic aneurysm can be repaired by resection of fibrous exteriorised scar followed by direct suture of the "neck" of the aneurysm.
2. When the septum is widely involved, geometric reconstruction is the best solution in a great majority of cases. Linear repair produced poor physiological results (28). Jakob et al. (29), Grossi et al. (30), Lundblad et al. (31) are among authors that have reported positive experiences with endoventricular plasty and geometric repair over the past 15 years. Interestingly, Shapira et al. (32), Kesler et al. (33), Tavakoli et al. (34), showed no difference in the results between linear suture and patch repair. The reasons for equivocal results between two distinctly different techniques might be due to
3. The retrospective nature of the comparisons,
4. Small number patients in each series,
5. The procedure being used only on dyskinetic bulging aneurysms.
6. The series often spanning a long time period
7. Left ventricular ejection fraction is used to report the data, without detailed information on the technique of assessment (angiography, radioisotope, or echocardiography) or ventricular volume measurements. The imaging techniques are often not consistent and, therefore, not comparable.
8. Some suggestions have been made to improve poor results of linear suture. Stoney described a sandwich technique (35), for repairs of septal scars. Cooley described plication of the free ventricular wall in his original publication and this technique is still a very useful but fails to address the issue of the akinetic or dyskinetic septum. Mickelborough uses reinforcement of the septum with a patch (36) and also advocates a tailored "convergent suture" from outside to inside to reduce the length of the vertical suture.
9. Athanasuleas and Buckberg promoted beating heart repair during the ventricular repair phase of the operation in an attempt to better preserve ventricular function and to also assess areas of potentially viable myocardium by palpation (37). There are many advantages and disadvantages of beating heart repair. The theoretically benefits of a perfused myocardium over cardioplegic arrest, may not be clinically obvious in the majority of patients (38). Some of the contentious discussion points are:

   (a) The exact location and the extent of the asynergic area cannot be reliably and reproducibly identified by palpation alone. The extent of scar should be carefully analysed pre-operatively on imaging studies with multiple projections and a plan formed as to the actual areas that need to be excluded.
   (b) Diastolic balloon sizing of the residual left ventricle is more cumbersome when performed on a beating heart. This may be an important step for inexperienced or occasional surgeons, to ensure good early and intermediate results.

8.5.2. Adjunctive Therapies in Ischemic Cardiomyopathy

1. Medical treatment with the appropriate medications form the cornerstone of chronic management (39). Many of the drugs have a positive impact on controlling symptoms and reducing the metabolic demand on the heart, thereby allowing greater efficiency of cardiac function. Newer approaches such cardiac resynchronization or bi-ventricular pacing may be effective in about one third of ischemic patients, with a potential improvement of 1.5% to 5% in EF without any effect on one year mortality (40).
2. Improving blood flow to the ischemic areas with percutaneous intervention or surgical revascularisation, without addressing the enlarged heart, does not significantly improve dilated ischemic myocardium (41).
3. There is much promise in the arena of cellular therapy, during acute, healing and the chronic phases after myocardial infarction. The hope is that this will reduce the extension of the scar, and prevent remodelling. None of the trials of regenerative therapy have been significant clinically (42).

DropBooks

4. There is a revolution in the realm of mechanical assistance with a variety of small pumps that show great promise. For the moment, these devices are building on the promise shown by the Heartmate in the REMATCH trial (43).
5. Ventricular containment or passive constraint maybe of interest in the treatment of dilated cardiomyopathies (44). Containment of a reconstructed scar with the addition of cellular regenerative therapy maybe a future therapy to watch,. This may even be applied early after a myocardial infarction to reduce remodelling and improve borderzone function (45).

Key Points to Remember

- Left ventricular volume, not ejection fraction determines prognosis in dilated ventricles after myocardial infarction.
- Left ventricular reconstruction began with repair of left ventricular aneurysms in the 1950s by the linear closure technique.
- The contributions of Dor and Jatene suggested that the best approach would be to attempt to recreate the conical shape of the left ventricle.
- Jatene's proposed imbrication of the septum to eliminate dyskinesia of this segment. Geometric principles essentially utilize small patches of various kinds or purse string sutures to get reshape the ventricle into a conical form.
- Reconstruction of scarred ventricles should be advocated soon after the ventricle dilates without waiting for symptoms of heart failure and decompensation.
- Reconstructive therapies owe their success to a combination of modification of the anatomical deformation of the dilated ventricle, physiologic improvement of geometric efficiency and appropriate medical therapies.

References

1. Likoff W, Bailey CP. Ventriculoplasty: excision of myocardial aneurysm. JAMA 1955; 158:915.
2. Cooley DA, Collins HA, Morris GC, et al. Ventricular aneurysm after myocardial infarction: surgical excision with use of temporary cardiopulmonary bypass. JAMA 1958; 167:557.
3. Josephson ME, Harken AH, Horowitz LN. Endocardial excision: a new surgical technique for the treatment of recurrent ventricular tachycardia. Circulation 1979; 60:1430–1439.
4. Klein MD, Herman MV, Gorlin R. A hemodynamic study of left ventricular aneurysm. Circulation 1967; 35:614–630.
5. Dor V, Kreitmann P, Jourdan J, Acar C, Saab M, Coste P. Interest of physiological closure (circumferential plasty on contractile areas) of left ventricle after resection and endocardectomy for aneurysm of akinetic zone comparison with classical technique about a series of 209 left ventricular resections (abstract). J Cardiovasc Surg 1985; 26:73.
6. Jatene AD. Left ventricular aneurysmectomy resection or reconstruction. J Thorac Cardiovasc Surg 1985; 89:321–331.
7. Fujimura T, Kawaguchi AT, Ishibashi-Ueda H, Bergsland J, Koide S, Batista RJ. Partial left ventriculectomy for patients with ischemic cardiomyopathy. J Card Surg 2001(Mar–Apr); 16(2):145–152.
8. Braunwald E, Pfeffer M. Ventricular enlargement and remodeling following acute myocardial infarction: mechanisms and management. Am J Cardiol 1991; 68(Suppl D):1D–6D.
9. Packer M. The neurohormonal hypothesis: a theory to explain the mechanism of disease progression in heart failure. J Am Coll Cardiol 1992; 20:248–254.
10. Christian T, Behrenbeck T, Gersh B, et al. Relation of left ventricular volume and function over one year after acute myocardial infarction to infarct size determined by technetium-99 m sestamibi. Am J Cardiol 1991; 68:21–26.
11. Chareonthaitawee P, Christian TF, Hirose K, et al. Relation of initial infarct size to extent of left ventricular remodeling in the year after acute myocardial infarction. J Am Coll Cardiol 1995; 25:567–573.
12. Fieno D, Raymond P, Kim J, Chen EL, et al. Contrast-enhanced magnetic resonance imaging of myocardium at risk. JACC 2000; 36(6):1985–1991.
13. Rehwald W, Fieno D, Chen EL, et al. Myocardial magnetic resonance imaging contrast agent concentrations after reversible and irreversible ischemic injury. Circulation 2002; 105:224–229.
14. Bogaert J, Maes A, Van de Werf F, et al. Functional recovery of subepicardial myocardial tissue in transmural myocardial infarction after successful reperfusion. Circulation January 1999; 36–43.
15. Gaudron P, Eilles C, Kugler I, et al. Progressive left ventricular dysfunction and remodeling after myocardial infarction. Potential mechanisms and early predictors. Circulation 1993; 87:755–763.
16. White HD, Norris RM, Brown MA, et al. Left ventricular end-systolic volume as the major determinant

of survival after recovery from myocardial infarction. Circulation 1987; 76:44–51.
17. Yamaguchi A, Ino T, Adachi H, et al. Left ventricular volume predicts postoperative course in patients with ischemic cardiomyopathy. Ann Thorac Surg 1998; 65:434–438.
18. Parrino PE, Kron IL. RESTORE Group: The role of left ventricular reconstruction in cardiogenic shock. Semin Cardiothorac Surg 2001; 13(4):476–479.
19. Dor V, Saab M, Kornaszewska, et al. Left ventricular aneurysm: a new surgical approach. Thorac Cardiovasc Surg 1989; 37:11–19.
20. Dor V, Di Donato M, Sabatier M, et al. Left ventricular reconstruction by endoventricular circular patch plasty repair: a 17-year experience. Seminars 2001; 43:435–447.
21. Athanasuleas CL, Buckberg GD, Stanley AW, Siler W, Dor V, Di Donato M, Menicanti L, Almeida de Oliveira S, Beyersdorf F, Kron IL, Suma H, Kouchoukos NT, Moore W, McCarthy PM, Oz MC, Fontan F, Scott ML, Accola KA. RESTORE group. Surgical ventricular restoration in the treatment of congestive heart failure due to post-infarction ventricular dilation. J Am Coll Cardiol 2004(Oct 6); 44(7):1439–1445. J Am Coll Cardiol 2005(Aug 2); 46(3):562; author reply 562–563.
22. Dor V, Sabatier M, Di Donato M, et al. Late hemodynamic results after left ventricular patch repair associated with coronary grafting in patients with postinfarction akinetic or dyskinetic aneurysm of the left ventricle. J Thorac Cardiovasc Surg 1995; 110:1291–1301.
23. Di Donato M, Sabatier M, Toso A. Regional myocardial performance of non-ischaemic zones remote form anterior wall left ventricular aneurysm. Effects of aneurysmectomy. Eur Heart J 1995; 16:1285–1292.
24. Di Donato M, Sabatier M, Dor V, et al. Effects of the Dor procedure on left ventricular dimension and shape and geometric correlates of mitral regurgitation one year after surgery. The J Thorac Cardiovasc Surg 2001; 121(1):91–96.
25. Tanoue Y, Ando H, Fukumura F, et al. Ventricular energetics in endoventricular circular patch plasty for dykinetic anterior left ventricular aneurysm. Ann Thorac Surg 2003.
26. Shenk S, McCarthy P, Starling R, et al. Neurohormonal response to left ventricular reconstruction surgery in ischemic cardiomyopathy. J Thoracic Cardiovasc Surg 2004; 128:38–43.
27. Beck C. Operation for aneurysm of the heart. Ann Surg 1944; 120:34.
28. Froehlich RT, Falsetti HL, Doty DB, et al. Prospective study of surgery for left ventricular aneurysm. Am J Cardiol 1980; 45:923.
29. Jakob H, Zölch B, Schuster S, et al. Endoventricular patch plasty improves results of LV aneurysmectomy. Eur J Cardiothorac Surg 1993; 7:428–436.
30. Grossi E, Chimitz L, Galloway A, et al. Endoventricular remodeling of left ventricular aneurysm: functional, clinical and electrophysiological results. Circulation 1995; 92(Suppl II):98–100.
31. Lundblad R, Abdelnoor M, Svennevig JL. Repair of left ventricular aneurysm: surgical risk and long-term survival. Ann Thorac Surg 2003; 76:719–725.
32. Shapira O, Davidoff R, Hilkert R, et al. Repair of left ventricular aneurysm: long-term results of linear repair versus endoaneurysmectomorrhaphy. Ann Thorac Surg 1997; 63:401–405.
33. Kesler KA, Fiore AC, Naunheim KS, et al. Anterior wall left ventricular aneurysm repair. A comparison of linear versus circular closure. J Thorac Cardiovasc Surg 1992; 103:841–848.
34. Tavakoli R, Bettex A, Weber A, et al. Repair of post infarction dyskinetic LV aneurysm with either linear or patch technique. Eur J Cardiothorac Surg 2002; 22:129–134.
35. Stoney W, Alford W, Burrus G, et al. Repair of anteroseptal ventricular aneurysm. Ann Thorac Surg 1973; 15:394.
36. Mickleborough L, Merchant N. Left ventricular reconstruction: early and late results. J Thorac Cardiovasc Surg 2004; 128:27–37.
37. Athanasuleas C, Buckberg G, Stanley A, et al. Surgical ventricular restoration in the treatment of congestive heart failure due to post-infarction ventricular dilatation. J Am Coll Cardiol 2004; 44:1439–1445.
38. Maxey TS, Reece TB, Kron IB, et al. The beating heart approach is not necessary for the Dor procedure. Ann Thorac Surg 2003; 76:1571–1575.
39. Braunwald E, Bristow M. Congestive heart failure: fifty years of progress. Circulation 2000; 102(20 Suppl 4):IV14–23.
40. St John Sutton M, Plappert T, Abraham W, et al. Effect of cardiac resynchronization therapy on left ventricular size and function in chronic heart failure. Circulation 2003; 107:1985–1990.
41. Bax J, Schinkel A, Boersma E, et al. Extensive left ventricular remodeling does not allow viable myocardium to improve in left ventricular ejection fraction after revascularization and is associated with worse long-term prognosis. Circulation 2004; 110(Suppl II):II-18–II-22.
42. von Harsdorf R, Poole-Wilson P, Dietz R. Regenerative capacity of the myocardium: implications for treatment of heart failure. Lancet 2004; 363:1306–1313.
43. Dembitsky W, Tector A, Park S, et al. Left ventricular assist device performance with long-term circulatory support: lessons from the REMATCH trial. Ann Thorac Surg 2004; 78:2123–2130.

DropBooks

44. Raman J, Power JM, Buxton BF, et al. Ventricular containment as an adjunctive procedure in ischemic cardiomyopathy: early results. Ann Thorac Surg 2000; 70:1124–1126.
45. Blom AS, Pilla JJ, Arkles J, Dougherty L, Ryan LP, Gorman II JH, Acker MA, Gorman RC. Ventricular restraint prevents infarct expansion and improves borderzone function after myocardial infarction: A study using magnetic resonance imaging, three-dimensional surface modeling and myocardial tagging. Ann Thor Surg 2007; 84:2004–2010.

9
Modifications of the Dor Procedure and Failure Modes of the Procedure

Jai Raman

Many modifications of the classic Dor procedure of left ventricular reconstruction exist and have been developed. These next few paragraphs will deal with a few modifications. The latter half will deal with the failure mode of the Dor procedure and evolution of some of the modifications based on those failures.

One of the basic tenets of left ventricular reconstruction is an attempt to recreate the conical shape of the heart. If one can imagine the dyskinetic or scarred region expanding from a small area of scar, reducing the dead space occupied by the scar would be a fundamental principle. In the Dor procedure, the healthy edges of the ventricle adjacent to the scar are brought closer together with a circumferential purse-string suture called the Fontan stitch. The patch was then sutured to the edges of the tightened scar. Patrick McCarthy, while at the Cleveland Clinic, proposed a modification which utilized only the stitch and avoided the patch. Figure 9.1 shows the aneurismal anteroapical scar and figure 9.2 shows the principles of the McCarthy modification.

Complex ventricular reconstruction (CVR) is now being employed. Much has been written about the techniques and the patients who benefit from this kind of surgical technique. Little is mentioned about the patients who have a poor outcome. In any kind of new procedure, case selection is important to achieve optimal results. We therefore studied the failure mode of left ventricular reconstructive procedures over an 8-year period in three major hospitals in two continents to identify risk factors in these patients. The principles that Dr. Dor described earlier in this chapter were utilized and modified as our experience evolved. In addition, there were simplications like the McCarthy modification which could be used in smaller scars.

Figure 9.3 shows the McCarthy modification along with a septal plication. For purposes of illustration, we describe a retrospective study that looked at the adverse outcomes of left ventricular reconstructive techniques. The lessons learnt provide several valuable lessons in the way these techniques should be utilized. We studied all patients who underwent geometric left ventricular reconstructive procedures from 1997 to 2005 at the University of Melbourne hospitals, University of Hobart hospital and the University of Chicago hospitals. All patients who underwent a left ventricular reconstruction (modified Dor procedure) were included. The steps required in the left ventricular reconstruction are outlined in the figures.

Figures 9.4–9.6 describe the philosophy of left ventricular reconstruction using a geometric approach utilizing the principles outlined by Dor and Cooley, which we had described earlier.[1]

Figures 9.7 and 9.8 show septal dyskinesis and septal plication with a suture. Figure 9.9 shows a patient who has septal plication and implantation of a bovine pericardial patch. Patient data were gleaned from hospital records, outpatient records and follow-up investigations. Patients were included regardless of the acuity and mode of presentation. Peri-operative outcomes were measured and post-operative complications tabulated. When mortality occurred, post-mortem examinations were requested and the results recorded. Complications were classified as fatal and non-fatal. All deaths

DropBooks

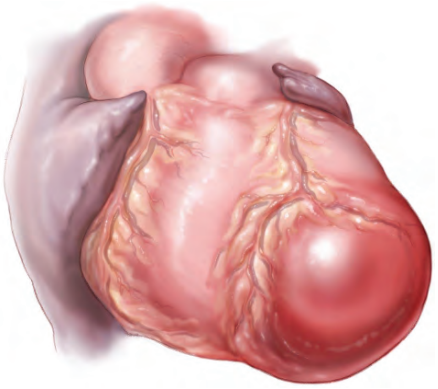


FIGURE 9.1. An apico-lateral left ventricular scar.

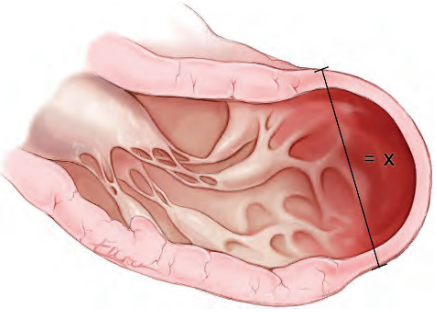


FIGURE 9.4. Longitudinal section of a dilated left ventricle with an apical scar.

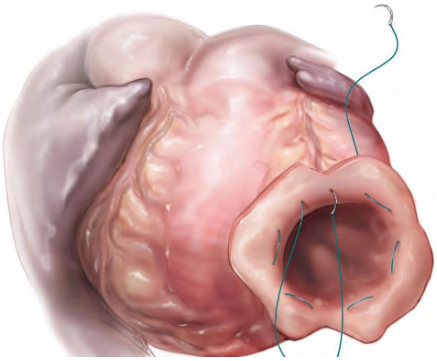


FIGURE 9.2. Purse-string suture along the borderzone, as proposed by McCarthy.

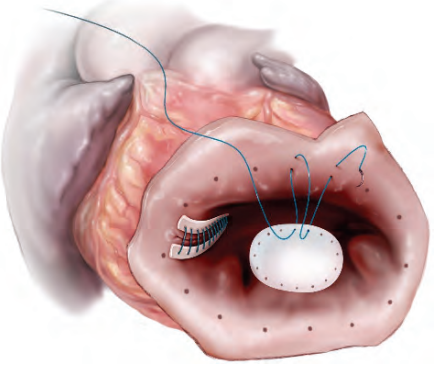


FIGURE 9.5. End-on view of opened apical scar with implantation of pericardial patch. Note the plicated septum and the radially placed sutures from the patch to the healthy myocardium beyond the scarred edges.

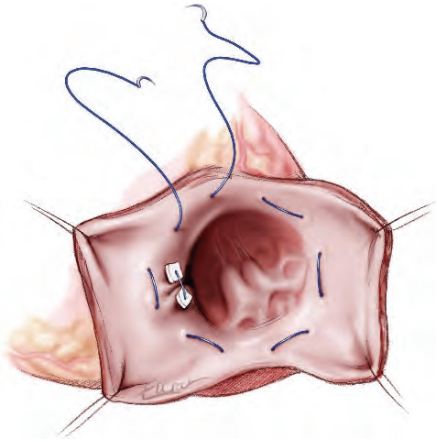


FIGURE 9.3. Combined McCarthy repair and septal plication: The septum has been plicated, followed by the purse-string suture along the healthy borderzone at the edge of the opened scar.

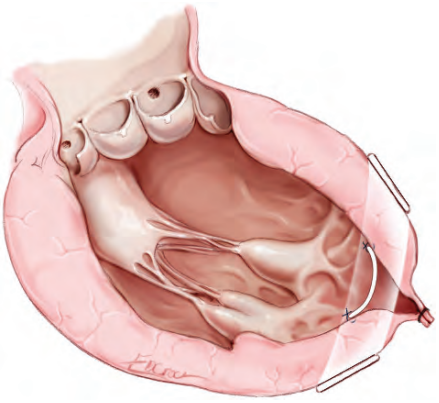


FIGURE 9.6. Completed repair shown in longitudinal section. Note the patch on the inside and the teflon strips on the outside.

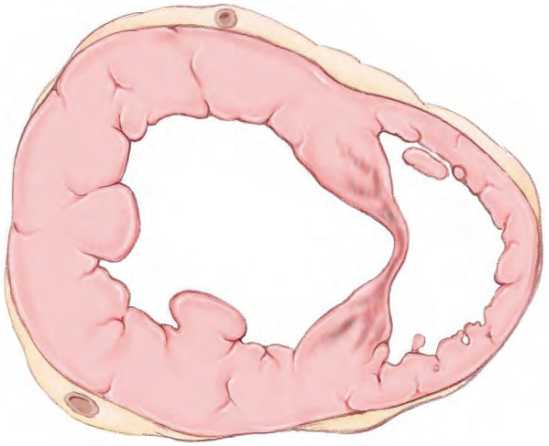


FIGURE 9.7. Cross section of ventricles showing septal scar with dyskinesis.

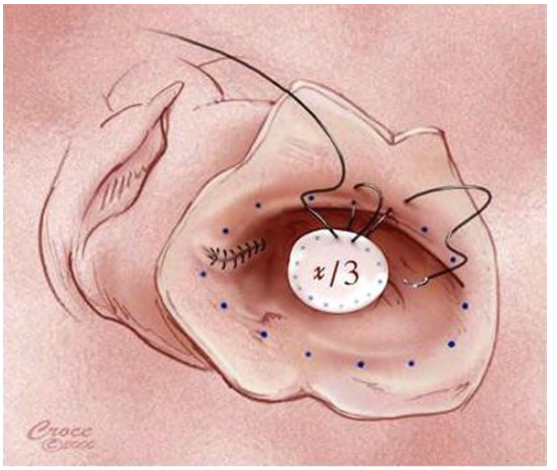


FIGURE 9.9. End-on view of ventricular reconstruction, showing the septal plication on the left with patch repair.

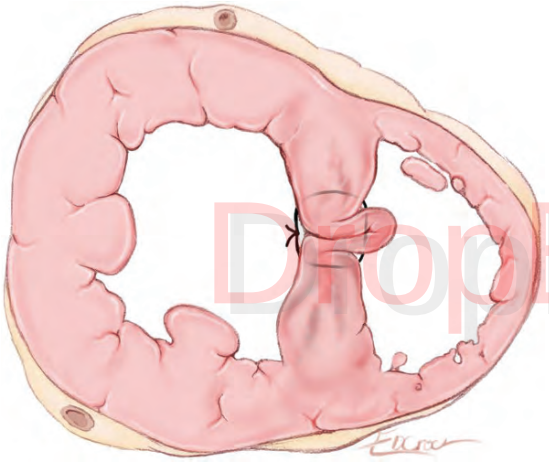


FIGURE 9.8. Schematic diagram showing septal plication with a suture.

as a consequence of the surgery, however remote, were recorded to derive the operative mortality. Non-fatal complications included the following:

Low cardiac output
End-organ dysfunction, such as renal failure and liver dysfunction
Ventricular arrhythmias
Neurological dysfunction, including transient ischemic attack (TIA), stroke, etc.
Persistent congestive heart failure
Prolonged respiratory support as a consequence of cardiac decompensation
Persistent cardiac failure
Need for prolonged ventricular assistance

Recurrence of cardiac failure and late decompensation, if any, were recorded. Where possible, patients were followed by heart failure cardiologists or a service dedicated to looking after patients with heart failure. Patients were reviewed every 6–12 months clinically where possible. Repeat echocardiography was advised to all patients. All adverse events were recorded. In the absence of contact or follow-up, attempts were made to contact referring physicians to accurately obtain quality of life information and late complications, if there were any.

Between January 1997 and February 2005, 284 patients underwent left ventricular reconstruction. Mean ejection fraction was 24.5 ± 7%. Mean New York Heart Association (NYHA) functional class was 3.2. All of the procedures were performed as adjuncts to coronary artery surgery and/or valvular surgery. Patients were followed up clinically and/or echocardiographically. Failure modes were classified as fatal or non-fatal. Non-fatal failure mode was defined as either persistent heart failure, recurrence of left ventricular scar, need for ventricular assistance, persistent ventricular arrhythmia or a combination.

DropBooks

9.1. Results

Operative mortality rate (OMR) was defined as peri-operative death or death as a complication of the surgical procedure, regardless of length of hospital stay. Operative mortality was 8% (23 deaths). This fatal failure mode was most related to urgency of surgery and cardiogenic shock in 15 patients (5.3% of OMR), stroke in 5 patients (1.8%) or post-operative biventricular failure in 3 (1%). In this category, most of the patients (n = 17) were in established cardiogenic shock with a combination of inotropes, pressors and balloon counterpulsation. Surgery was performed as an emergency or on an urgent basis. This was often in the setting of an acute infarct complicating an already poor ventricle. Post-operative biventricular failure was seen in three patients that was prolonged and required delayed implementation of ventricular assistance, often in the setting of intractable post-operative ventricular arrhythmias.

Unexpected intra-ventricular clot was found in four patients despite good quality pre-operative echocardiography and intra-operative trans-oesophageal echocardiography. The nature of the clot was often friable and soft, and this made them embolize relatively easily. The size of each of these clots was over 3 cm, representing a failure of trans-oesophageal echo in recognizing these early soft thrombi. The embolism occurred despite minimal manipulation of the heart before ventriculotomy.

Non-fatal failure modes (NFM) accounted for morbidity in 26 patients (9%). This was predominantly due to persistent septal dyskinesis in seven patients (2.46%), persistent mitral regurgitation in five (2.5%), post-operative ventricular tachycardia in four (1.4%), sub-optimal myocardial protection in four (1.4%) and use of a large, stiff patch in four (1.4%).

Persistent septal dyskinesis resulted in discoordinate ventricular contraction with only partial improvement in ventricular function. This was despite using a patch to exclude the septal component of the scar. This was also early in the experience. Complete coverage of a large area of septal dyskinesis with a patch was often difficult.

Persistent mitral regurgitation was seen in five patients. All of these patients had multiple patchy scars with some remodelling of the infero-basal wall. The mechanism of MR was due to an akinetic or sluggish infero-basal ventricular wall. These patients had moderate mitral regurgitation which was left alone at the time of surgery, because of the lack of consensus on what to do about these patients.

Early in the experience, we followed the principles described by Dor. The Dacron patch was stiff and tended to almost stent open the area to be reconstructed. This invariably resulted in a sub-optimal result with residual heart failure. Over the early phase of this experience, we moved from Dacron to Goretex patches and settled down to using Bovine Pericardial patches (Supple Perigard™, manufactured by Synovis Biomedical Inc., St. Paul, MN).

Post-operative ventricular tachycardia was seen in four patients. In two of these patients, it was profound and early in the post-operative period. In one of these patients, it caused profound hemodynamic compromise, requiring mechanical assistance with extra-corporeal membrane oxygenation (ECMO). The ventricular tachy-arrhythmia slowly resolved after 48 h. However, the patient had an embolic episode during his period of assistance and support was withdrawn despite a reasonable chance of cardiac recovery.

In two patients, there were late episodes of ventricular tachy-arrhythmia, both of which were at home. Both patients were successfully resuscitated, cardioverted and admitted for insertion of automatic internal cardioverter defibrillators (AICD). Since then, our policy in treating these patients has changed. Any patient with a pre-existing history of ventricular arrhythmia gets an endocardial ablation at the borderzone. If patients have any post-operative ventricular arrhythmias, they undergo an electrophysiological study. The threshold for electrophysiological intervention now is quite low.

Four patients spent a long time recovering from surgery with gradual resolution of cardiac failure. These patients had predominantly right sided cardiac failure which was presumably because of inadequate myocardial protection of the right coronary artery territory during the cross-clamp period. We have changed our techniques over the past 100 patients to avoidance of the cross-clamp and cardioplegia. If there is a large clot and the cross-clamp is required, this is done first followed by myocardial revascularization, which is then performed on a beating heart.

The use of a stiff and relatively big patch (4–5 cm in diameter) accounted for significant

morbidity in four patients. Two of these patients presented with localized recurrence near the edge of the patch. In one of them, this was the focus of ventricular tachycardia. In two other patients, the patch seemed to be associated with progression of mitral regurgitation from mild to moderate.

One hundred and ninety-nine of the surviving 261 patients (76%) were in NYHA class I. Twenty patients were lost to follow-up. All patients in NYHA class I were maintained on a combination of angiotensin-converting enzyme (ACE) inhibitors, beta blockers and diuretics. There were no instances of recurrent ischemia or heart failure decompensation in this group.

Unfortunately, there was no control group to perform robust statistical comparisons. While data were collected prospectively, this was a retrospective review of the data.

Ventricular reconstruction was initially a technique used predominantly for repairing ventricular aneurysms. Linear repair of aneurysms was the accepted norm for almost three decades thereafter.[2,3] Despite the relative ease of these procedures popularized by Cooley,[4] the peri-operative complications gave ventricular aneurysm repair a bad name. Dr Jatene[5] and Dr. Dor[6] independently showed the importance of a geometric approach to repairing the left ventricle in such a way that the conical shape is recreated. The improved results with a circular repair or a geometric approach have now been well accepted for over a decade.[7] The next phase in the evolution of left ventricular reconstructive surgery was to address not just frankly aneurismal or dyskinetic anterior ventricular scars but to attempt correction in cases where there was akinesis of a large confluent anterior left ventricular scar.[8] As percutaneous treatment of acute coronary syndromes has improved all over the world, truly ventricular aneurysms have become more uncommon. There is also the appreciation based on the Surgical Trial in Intracerebral Haemorrhage STICH trial (Surgical Treatment of Ischemic Heart Failure) that aggressive myocardial revascularization alone cannot alter the function and shape of a ventricle remodelled by infarction.[9] However, the physiological effects of geometric left ventricular reconstruction have been successfully applied to post-ischemic akinetic dilatation of the left ventricle.[10]

Across the board, the operative mortality in these sick patients ranges from 7% to 12%.[11-13] Many of these publications have focused rightly on the positive outcomes of these reconstructive procedures. This is particularly important as the incidence of heart failure increases and there is greater acceptance of the role of left reconstructive procedures in the surgical armamentarium.[14] While the surgical community is embracing these new techniques with greater enthusiasm, appropriate case selection is very important.

We present our experience with left ventricular reconstruction over an 8-year period encompassing 284 patients at three institutions in two continents. We presented some of our learning experiences to help improve the surgical technique to accommodate all types of patients.

On the basis of our experience, we now know that left ventricular reconstruction in the presence of cardiogenic shock or as an emergent procedure carries a considerable risk of mortality. If there is end-organ failure, our strategy now is to connect the patient to some kind of mechanical ventricular assistance. We routinely advocate insertion of an intra-aortic balloon pump pre-operatively, if one has not been inserted already. We also have a low threshold for insertion of a ventricular assist device as the patient is being weaned off cardiopulmonary bypass.

To reduce myocardial dysfunction in these patients, we have also switched to performing most of these procedures on cardiopulmonary bypass with the heart beating. The only caveat to that is when there is evidence of ventricular clot on echocardiography. In those instances, we use the cross-clamp and cardioplegic arrest early to allow reconstruction of the ventricle with safe extraction of the thrombus. Thereafter, we tend to perform the coronary artery bypass procedures with the heart beating, thereby limiting the cross-clamp period. This has also reduced the need for post-cardiotomy mechanical ventricular support for inadequate myocardial protection.

Ventricular arrhythmias can frequently be a complication and cause of poor outcome in patients undergoing left ventricular reconstruction. We have adopted various techniques to reduce the incidence of these arrhythmias post-operatively, ranging from intra-operative ablation of the endocardium to electrophysiology studies and insertion of AICDs.[15] Extensive work has been done by Dor[16] in this area and we follow most of his principles in dealing with ventricular arrhythmias.

DropBooks

The use of a stiff patch was interestingly associated with some adverse long-term outcomes, which included recurrent scar formation at the edge of the patch, and progression of mitral regurgitation. We have since completely switched to using small bovine pericardial patches to help recreate the conical shape of the ventricle. The septal component of the scar is now routinely plicated in a linear fashion using techniques promulgated by Jatene. This has allowed an even better geometric reconstruction of the ventricle.

This publication is an attempt to identify some of the common complications following left ventricular reconstruction and our measures to reduce some of these effects. Our follow-up to this would be to analyse these failure modes, using more sophisticated statistical methods such as propensity scores.

Useful tips and Pitfalls to Avoid in Surgery

Left ventricular reconstruction in patients with an acute MI or in cardiogenic shock, is associated with a high mortality and should be conducted is special circumstances.

Containment or constraint devices might be of greatest use in the acute infarct setting or within the first three to four weeks after an infarct.

The use of magnetic resonance imaging and 3 Dimensional echocardiography assist in making better determination of how the ventricle should be re-shaped (reverse remodeling).

A small leak between the patch and the excluded LV cavity when it is visualized in the OR, can be ignored if small. Larger leaks need to be addressed by refashioning of the patch. Interrupted sutures or multiple overlapping running sutures may be very useful.

Moderate mitral regurgitation should preferably be repaired. Occasionally, the mitral valve may be repaired or replaced through the left ventricle if it is a large scar. The Alferi stitch is associated with sub-optimal long term outcomes.

Use of pre-and peri-operative Amiodarone to helps decrease incidence of lethal arrhythmias.

Avoid beating heart reconstruction in frail old patients with fragile tissues. If there is any suspicion of clot, this technique should not be used.

Key Points to Remember

- Left ventricular reconstruction utilizes the principles elucidated by Dor and Jatene, in an attempt to geometrically reconstruct the conical shape of the heart.
- Smaller infarcts may be excluded by purse-string sutures.
- Larger scars over 4 cm in diameter may best be addressed by a small patch.
- The scarred remnants can be approximated over the patch.
- A flexible and pliable patch with a material like bovine pericardium provides the best handling capabilities.
- These patients are best handled as complex heart failure patients and managed as such.
- Surgery early after an infarct is associated with a high complication rate.

References

1. Raman J, Sakaguchi G, Buxton BF. Outcome of geometric endo-ventricular repair in impaired left ventricular function. *Ann Thorac Surg*. 2000;70:1127-1129.
2. Shaw RC, Ferguson TB, Weldon CS, Connors JP. Left ventricular aneurysm resection: Indications and long-term follow-up. *Ann Thorac Surg*. 1978;25:3336-3339.
3. Barratt-Boyes BG, White HD, Agnew TM, Pemberton JR, Wild CJ. The results of surgical treatment of left ventricular aneurysm: An assessment of the risk factors affecting early and late mortality. *J Thorac Cardiovasc Surg*. 1984;87:87-98.
4. Reddy SB, Cooley DA, Duncan JM. Left ventricular aneurysm: Twenty year surgical experience with 1572 patients at the Texas Heart Institute. *Cardiovasc Dis Bull Tex Heart Inst*. 1981;11:165-186.
5. Jatene AD. Surgical treatment of left ventricular aneurysm. In: Baue AE, Geha AS, Hammond GL, Laks H, Naunheim KS (eds.), *Glenn's Thoracic & Cardiovascular Surgery*. Vol. 2, 5th edn. Norwalk, CT: Appleton & Lange; 1991:1829-1836.
6. Dor V, Saab M, Coste P, Kornaszewska M, Montiglio F. Left ventricular aneurysm: A new surgical approach. *Thorac Cardiovasc Surg*. 1989;37:11-19.
7. Kesler KA, Fiore AC, Naunheim KS. Anterior wall ventricular aneurysm repair: A comparison of linear versus circular closure. *J Thorac Cardiovasc Surg*. 1992;103:841-848.
8. Dor V, Sabatier M, DiDonato M, Saab M. Late hemodynamic results after left ventricular patch repair associated with coronary grafting in patients with post-infarction

akinetic or dyskinetic aneurysm of the left ventricle. *J Thorac Cardiovasc Surg*. 1995;110:1291-1301.
9. Menicanti L, Di Donato M. Surgical left ventricle reconstruction, pathophysiologic insights, results and expectation from the STICH trial. *Eur J Cardiothorac Surg*. 2004;26(suppl 1):S42–S46; discussion S46-S47.
10. Dor V. Reconstructive left ventricular surgery for post-ischemic akinetic dilatation. *Semin Thorac Cardiovasc Surg*. 1997;9(2):139-145.
11. Komeda M, David TE, Malik A, Ivanov J, Sun Z. Operative risks and long-term results of operation for left ventricular aneurysm. *Ann Thorac Surg*. 1992;53:22-28.
12. Sartipy U, Albage A, Lindblom D. The Dor procedure for left ventricular reconstruction. Ten-year clinical experience. *Eur J Cardiothorac Surg*. 2005;27(6):1005-–1010. Epub 2005 Feb 26.
13. Yamaguchi A, Adachi H, Kawahito K, Murata S, Ino T. Left ventricular reconstruction benefits patients with dilated ischemic cardiomyopathy. *Ann Thorac Surg*. 2005;79(2):456-461.
14. Mickleborough LL, Merchant N, Provost Y, Carson S, Ivanov J. Ventricular reconstruction for ischemic cardiomyopathy. *Ann Thorac Surg*. 2003;75(6 suppl):S6-S12.
15. Wellens F, Geelen P, Demirsoy E, et al. Surgical treatment of tachyarrhythmias due to postinfarction left ventricular aneurysm with endoaneurysmorrhaphy and cryoablation. *Eur J Cardiothorac Surg*. 2002;22(5):771-776.
16. Di Donato M, Sabatier M, Dor V, RESTORE Group. Surgical ventricular restoration in patients with postinfarction coronary artery disease: Effectiveness on spontaneous and inducible ventricular tachycardia. *Semin Thorac Cardiovasc Surg*. 2001;13(4): 480-485.

DropBooks

10
Mitral Valve Repair

Yoshikazu Suzuki, Martinus T. Spoor,* and Steven F. Bolling

10.1. Introduction

The management of patients with congestive heart failure (CHF) has become an international heath care problem and it is one of the world's leading causes of hospitalization and mortality. In our ever-aging population, advances in basic cardiac care that have extended our average life expectancy have also left more people living with chronic cardiac disease than ever before. In the United States alone, 4.9 million people (2.3% of total population) are suffering from heart failure with 550,000 new cases diagnosed each year. Hospital discharge for CHF increased from 377,000 in 1979 to 970,000 in 2002, an increase of 157%. Estimated health expenditures amount to US$25.3 billion in 2005.[1] In spite of these, only 2,100 of the 53,000 patients who die annually are offered transplantation, which many consider to be the standard treatment for selected patients with severe CHF and end-stage heart disease. Transplantation is severely limited by the paucity of donor availability and enormous cost. The inapplicability in the older patient or those with comorbid medical conditions as well as relatively fixed donor pool suggests that transplantation will likely never have a major epidemiological impact.[2] Treatment with mechanical circulatory support devices dances on the horns of the same dilemma. Consequently, despite improvements with medical management, 1-year, 3-year, and 5-year survival rates after hospitalization from CHF have been reported at ~60–80%, 50%, and 20–40%, respectively, which is worse than the prognosis of most cancers.[3–7]

In an effort to solve these problems, many alternative surgical and interventional strategies to treat heart failure patients have emerged and evolved over time. Some of them have been evaluated as the first-line approach to heart failure including techniques to restore myocardial perfusion and ventricular synchronization, to remodel ventricular geometry, and to eliminate mitral valve (MV) regurgitation (MR) in the setting of dilated cardiomyopathy (DCM).

Since 1993, we have been using MV repair techniques to help this patient population based on the assumption that the MV is the geometric functional component of the left ventricle (LV) and that secondary or functional MR occurs in the MV apparatus that is essentially normal and functional. The lack of effective function is reflective of a geometric problem of the LV. Secondary or functional MR can be thought of as geometric MR and we define MV repair of this geometric MR as geometric MV repair in this chapter. This chapter will examine the recent development and advancement of geometric MV repair which is now recognized as a safe and useful treatment option for heart failure in selective DCM patients, and will review the University of Michigan experience with geometric MV repair in cardiomyopathy.

10.2. MV Structure and Function

In order to address the issues of heart failure and MR, one needs to understand the complex anatomy and functional relationship of the LV and MV. MV

*Deceased.

competence depends on the coordinated function and geometry of the components of the MV apparatus: mitral annulus, mitral leaflets, chordae tendinae, papillary muscles, and importantly LV wall.[8–10] The most "efficient" function of LV depends on all the components of the LV and MV apparatus. There are substantial clinical and basic science evidences implicating the importance of preserving MV continuity and geometry in order to preserve the function of the LV.[11–13]

The MV is the inlet to the LV and can be mistakenly thought of as a "set of French doors." The anterior (septal/aortic) and posterior (mural) leaflets are "nominally" separated near the annulus by the posteromedial and anterolateral commissures. However, it should be noted that the leaflet part of MV is entirely continuous within the annulus much like a "curtain of a waterfall". The anterior leaflet is semicircular and spans the distance between the two commissures. At the portion of the annulus which serves as "hinge point" of both leaflets, the anterior leaflet is attached to the anterolateral wall of LV in the central region of the fibrous skeleton of the heart between the right and the left fibrous trigone where it is in direct continuity with the left end part of the noncoronary aortic valve leaflets. The posterior leaflet is rectangular in shape, and is divided into three portions by natural clefts in the leaflet. Figure 10.1 shows the relationship of the MV and its components to chords and papillary muscles.

The mitral annulus represents the junction that joins the left atrium and ventricle and consists of fibrous and muscular tissues. The average human mitral annular cross-sectional area is 5–11 cm^2. During systole, the annulus assumes an elliptical shape and is able to contract and decrease in diameter, whereas in diastole, it assumes a more circular shape. Annular flexibility allows for increased leaflet coaptation during systole and increased annular orifice area during diastole. The anterior aspect of the annulus, which is composed of the fibrous skeleton of the heart and consists of rigid but elastic fibrous tissues, has limited flexibility, whereas the posterior aspect of the annulus, which is in continuity with the fibrous skeleton and consists of a mixture of muscular and gradually tapering fibrous tissues, contributes most of the annular flexibility.

The chordae tendinae are composed of fibrous connective tissue chords and attach the leaflets directly to either the papillary muscles or the LV wall. The chordae are divided into three groups. The primary chordae attach directly to the free edge of the leaflet, and ensure that the leaflets coapt without prolapse or flail. The secondary chordae, which are more prominent on the anterior leaflet, attach to the leaflet along the line of coaptation, and are important in maintenance of ventricular function.[14] Tertiary chordae are present only on the posterior leaflet, and attach directly to the ventricular wall or to the trabeculae carnae. In addition, there are commissural chordae, which arise directly from either of the papillary muscles and attach to both leaflets.

The anterolateral and posteromedial papillary muscles project into ventricular cavity directly from the apical and mid portion of the ventricular wall, and give rise to chordae tendinae that attach to both leaflets. The anterolateral papillary muscle receives a dual blood supply from the left anterior descending and from either a diagonal or marginal branch of the circumflex artery. In contrast, the posterolateral papillary muscle has a singular blood supply, either from the right coronary or the circumflex artery. Therefore, the posteromedial aspect of the LV wall and the papillary muscle is more susceptible to ischemia and infarction and together play a very important role in valvular incompetence and leaflet malcoaptation in the instance of ischemic MR with a variable degree of posterior myocardial infarction.

The most important determinant of MV competency centers on the zone of coaptation (ZC). MV leaflets accommodate high systolic LV pressure and establish competence through the distribution of force that can be likened to the stresses in a "Roman arch" in order to lessen the stress to the other parts of the ventricle and MV apparatus. To maintain MV competency in a systolic phase, the adequate ZC needs to be established in a coordinated fashion. To achieve adequate coaptation, both anterior and posterior leaflets should

1. be close enough to each other,
2. have enough tissue to cover the length of the ZC, and
3. be guided at the line of coaptation by the chords at appropriate angle.

DropBooks

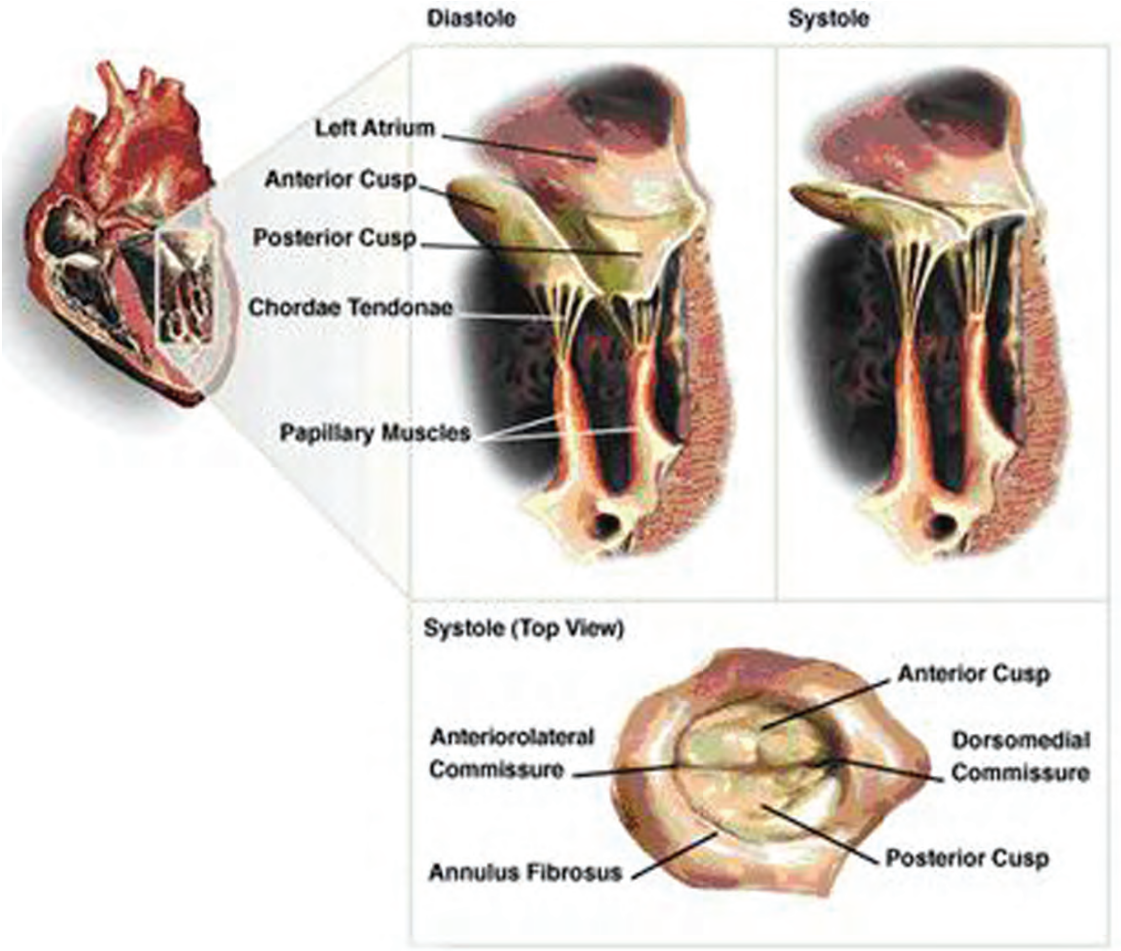


FIGURE 10.1. Anatomy—anterior and posterior leaflets of the mitral valve (MV).

10.2.1. Pathophysiology of MR

10.2.1.1. Acute MR Versus Chronic MR

In MR, the regurgitant volume which is ejected into the left atrium is dependent upon regurgitant orifice size, ventricular to atrial pressure gradient, atrial compliance, and heart rate. The degree of increase in left atrial pressure which is associated with congestive symptoms is significantly affected by the regurgitant volume and the compliance of the left atrium.

The compliance of the left atrium is much different between acute and chronic MR, so it is important to fully recognize and differentiate the chronicity of MR in each patient being evaluated with heart failure.

10.2.1.1.1. Acute MR

Causes of acute MR include chordal rupture, endocarditis, chest trauma, or myocardial infarction. The left atrium is of normal size with low compliance. A relatively small amount of acute MR can lead to an acute increase in left atrial pressure and lead to significant pulmonary edema that requires acute treatment. In this setting, symptoms dictate the proper timing of surgery.

10.2.1.1.2. Chronic MR

In chronic MR, there is a gradual increase in regurgitant flow into the left atrium that leads to atrial enlargement and a significant increase in left atrial

and pulmonary venous compliance. Therefore, signs and symptoms of pulmonary congestion may not become apparent until much later in the process of the disease in spite of the significant degree of MR and the significant volume overload and pathologic changes in the LV. In this setting, less symptomatic patients are difficult to triage in terms of proper timing of the intervention.[15] In this chapter, we treat geometric MR, which is chronic MR and a different disease entity from acute MR.

10.2.1.2. Valvular MR Versus Geometric MR

To understand the mechanism and the rational treatment of chronic MR, it is very useful to classify MR into primary/anatomic/valvular MR and secondary/functional/geometric MR.

In valvular MR, regurgitation is caused by structural valvular disease. The etiology of structural MV diseases include degenerative (myxomatous, namely, Barlow and fibroelastosis such as Marfan syndrome and connective tissue diseases), rheumatic, endocarditis, trauma, tumor, inflammatory, and congenital. In this setting, problems with the components of the MV apparatus cause MR.

DropBooks

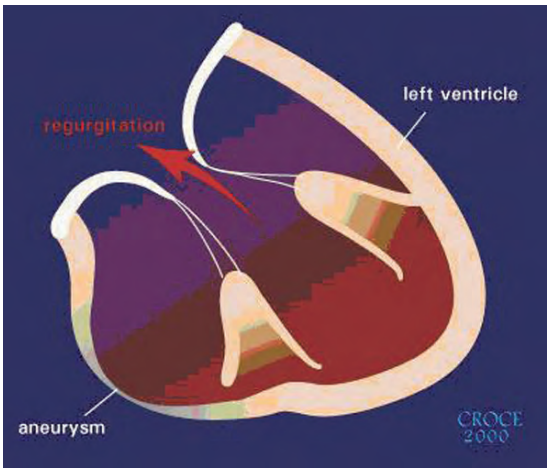


FIGURE 10.2. Mechanism of mitral valve regurgitation (MR) with inferobasal scarring of the left ventricle (LV). Note the remodeled inferobasal wall labeled "aneurysm" contributes to tethering of the posterior mitral leaflet, causing failure of coaptation of the mitral leaflets.

MV repair of this valvular MR is systematically guided by three functional anatomic categories of MV pathology proposed by Dr Carpentier in 1983[16]:

- annular dilatation
- leaflet prolapse with elongated or ruptured chordae
- leaflet restriction

The treatment of valvular MR aims to establish a ZC according to the functional anatomy. MV repair techniques in this setting include annuloplasty, variable degrees of leaflet resection, advancement or "sliding" plasty, chordal translocation, and polytetrafluoroethylene (PTFE, Gore-Tex®) neo-chordal implantation.

In contrast, secondary or geometric MR is defined as MR that is not caused by a structural defect of the components of the MV apparatus but rather is caused by a distorted functional position of the components of the MV apparatus related to LV dilatation. Therefore, geometric MR is not a valvular disease but a geometric ventricular disease. For example, LV dilatation of the secondary to an ischemic etiology with inferobasal akinesis or dyskinesis contributes to geometric MR. Figure 10.2 shows how inferobasal scarring and dyskinesis can contribute to MR.

DCM is defined by clinical evidence of chronic and progressive heart failure associated with findings of poor cardiac contractility and ventricular dilatation.

According to the primary etiology, DCM is usually classified into ischemic DCM and nonischemic DCM because ischemic DCM is most prevalent.

Nonischemic DCM can further be classified into idiopathic DCM (ventricular etiology) and valvular DCM (valvular etiology). It should be noted that there is a segment of this patient population that have concurrent ischemic heart disease and MR from degenerative MV disease at the same time, commonly seen in elderly patients. This group is distinct from patients with geometric MR with ischemic DCM.

In geometric MR, the components of the MV apparatus itself are normal; two of the three functional anatomic categories proposed by Dr Carpentier hold true:

- annular dilatation
- leaflet restriction: papillary muscle—LV wall displacement

Figure 10.3 shows the components of geometric MR. The treatment aim of geometric MR is to reestablish the ZC to eliminate regurgitation. To achieve this goal, a complete ring annuloplasty technique was initially used.[17] As surgeons be more comfortable with this technique, more and more aggressive undersizing and overcorrecting ring annuloplasty was used based on the assumption that the most significant determinant of leaflet coaptation in geometric MR is the diameter of the MV annulus and that undersizing, overcorrecting annulus would also help to compensate the widened angle and the septolateral distance of the papillary muscles from LV dilatation. These clinical observations and acceptable surgical results were correlated with several key echo parameters as well as improvement in symptoms and quality of life (QOL).[18–20]

The natural history of chronic degenerative or rheumatic valvular MR can be prolonged. The progression of the disease may be slow for several decades. The onset of symptoms is often masked and may present late in the progression of the disease even with elevated left atrial and LV end-diastolic pressures because of the slow, gradual progression of this process and the large compliant left atrium. The presence of MR contributes to increased back pressure and decreased forward flow as well.

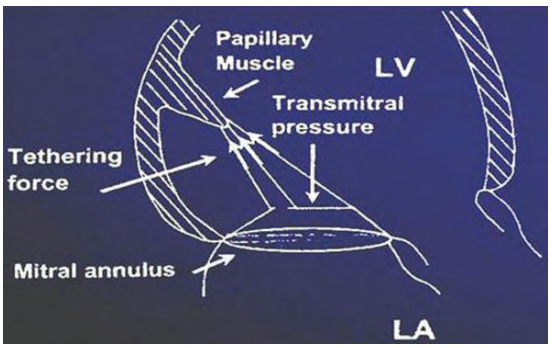


FIGURE 10.3. Various forces exerted on mitral valve (MV) leaflets are provided by the MV apparatus, papillary muscles, and important three-dimensional relationships in the ventricle itself of all of the associated structures. Geometric mitral regurgitation results from a combination of annular dilatation, papillary muscle displacement, increased leaflet tethering forces, and weakened leaflet closing forces.

Decreased forward flow is also compensated by an increased heart rate and total stroke volume that is the sum of regurgitant volume and effective forward stroke volume. This leads to increased workload from volume overload to the LV. Neurohormonal compensatory mechanism also play a role in maintaining effective forward stroke volume in the setting of chronic MR. The normal LV can accommodate a fairly large amount of regurgitant volume and can be well compensated before the LV starts to dilate. This is reflected in hyperdynamic wall motion and increased LV contractility. However, once increased volume overload reaches beyond the compensatory adaptation of the LV, the LV is forced to dilate through homeostatic compensation mechanisms. This is reflected in increased LV end-diastolic volume and dimension that results in increased LV wall tension and stress. The LV reacts to match increased wall tension by increasing the LV mass. As LV dilatation progresses, LV wall tension increases and coronary flow reserve decreases in addition to increased LV workload.[20–23] Increased LV wall tension is the most potent stimulus for progressive heart failure through the mechanism of LV remodeling at a genetic, molecular, and neurohormonal level. This chronic energy imbalance of increased workload, increased wall tension, and decreased coronary flow reserve accelerates the damage to the LV muscle and the loss of LV contractile functional reserve. The poor survival of patients with chronic degenerative MR and severe CHF symptoms has been well established. Even though total resistance to the LV is decreased by MR, the total workload to produce the same forward flow is proportionally increased to volume overload with MR. The development of clinical symptoms usually reflects significant LV dysfunction and is a hallmark of reduced life expectancy. In the current setting of low operative mortality and high feasibility of repair, the timing of MV repair can be offered at earlier stages of the disease in hopes of changing the natural history of the disease and before the development of left ventricular dysfunction.[15] A regurgitant volume of ≥ 60 ml per beat and effective regurgitant orifice area of $\geq 40\,mm^2$ are currently recommended as an index of quantitative assessment for the timing of MV repair in asymptomatic patients with degenerative valvular MR.[24,25]

Geometric MR with DCM further contributes to LV dilatation and remodeling through chronic phenotypical changes triggered by increased volume workload, increased LV wall tension, and decreased coronary flow reserve in addition to originally dysfunctional LV. This LV dilatation and spherical change further increases the magnitude of MR. Therefore, geometric MR sets up a vicious cycle and has been associated with worsened survival even with mild MR and few overt symptoms of heart failure.[26–28]

Compared to valvular MR, the natural disease progression of geometric MR is rapid and prognosis remains poor. Geometric MR is a prevalent complication of end-stage cardiomyopathy and may affect up to 60% of all heart failure patients as a preterminal or terminal event.[28–30] Ischemic MR, that is, geometric MR in ischemic DCM, doubles the mortality after myocardial infarction with a graded decrease in survival related to the severity of MR. Figure 10.4 reiterates the ischemic mechanism overlaid on the geometric components. It is reported that in ischemic DCM, the 5-year survival rate is 60% without MR, 45–50% with mild MR, and 30–35% with more than moderate MR.[31,32] Decreased LV function reflected in a decreased ejection fraction (EF) further predicts a worse prognosis.[33,34] The prognosis of ischemic DCM with MR is generally even worse than idiopathic DCM with MR.[28]

However, the appropriate timing of intervention for chronic, geometric MR is still very controversial because of the higher operative risk and poorly defined late outcome measures.

With normal ventricular geometry, the redundant mitral leaflets that are more than twice the area of the MV orifice are responsible for the ZC.[10] As the failing ventricle dilates, the multifactorial mechanisms of the progressive expansion of the mitral annulus and the dislocation of papillary muscles and LV wall lead to incomplete leaflet coaptation and a regurgitant jet of geometric MR.

DropBooks

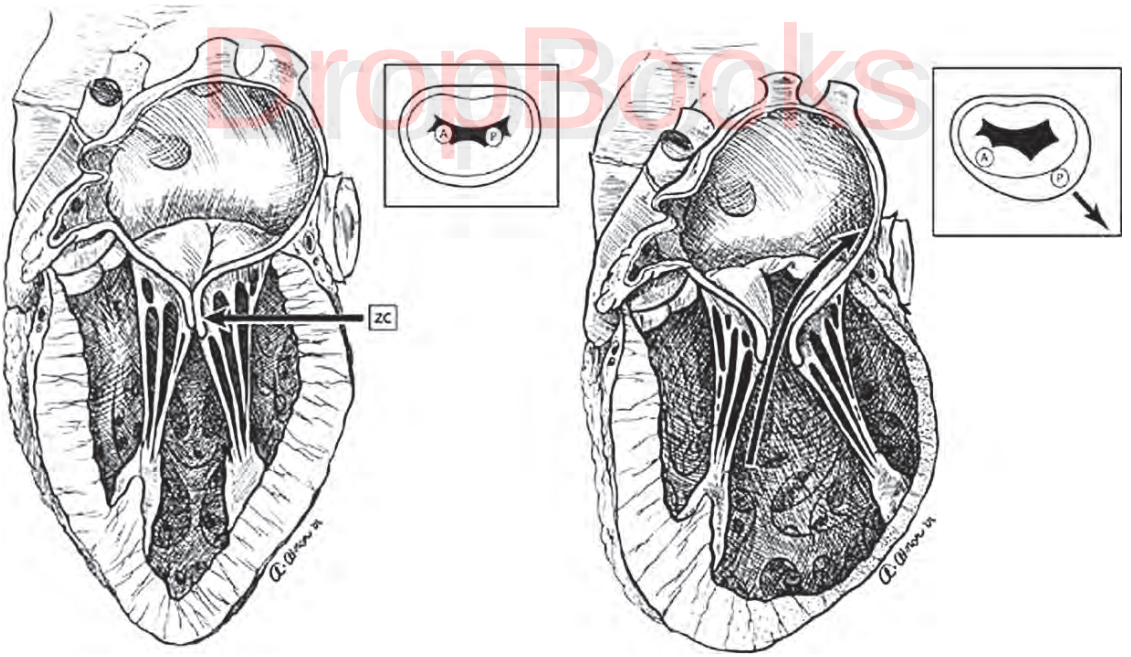


FIGURE 10.4. In ischemic cardiomyopathy, changes within the left ventricle (LV) may be asymmetric and still lead to functional mitral regurgitation. With ischemic damage and thinning of the ventricular wall, there is lateral tethering, displacement of the papillary muscle, and loss of the zone of coaptation (ZC), resulting in an eccentric jet of mitral regurgitation. This illustrates the concept that ischemic mitral regurgitation results from "lateral wall dysfunction" that, if left untreated, will progress to global LV dysfunction and severe heart failure.

As more leaflet tissue is utilized for coverage of the enlarging orifice, a critical reduction in leaflet tissue available for coaptation is reached so that leaflet coaptation becomes ineffective and that a central regurgitant jet type of geometric MR develops.[8,35,36] In studies of patients with idiopathic DCM, those with MR have significantly greater MV orifice area and significantly larger dimensions of the MV annulus than those without MR. Chordal length and papillary muscle length are not significantly different in patients with cardiomyopathy, with or without MR.[8] It is also reported that pharmacologic reduction in the dynamic MR by the medical treatment of heart failure was through a reduction in the regurgitant orifice area which was related to the decreased mitral annular distention.[36]

Therefore, the most significant determinant of leaflet coaptation in geometric MR is the diameter of the MV annulus. This forms the basis of the approach of the downsizing, complete ring MV annuloplasty. The spatial misalignment of the subvalvular MV apparatus, that is, papillary muscle–LV wall dislocation, also contributes to inability of leaflet coaptation.[9,37,38] As the ventricle dilates, the distance and the angle of the papillary muscles tends to become obtuse rather than acute, forcing the MV leaflet coaptation zone apart. In addition, there is a large apical force that pulls the papillary muscle and chordal apparatus in an inferior and lateral direction and there is a weak closing force of the poorly functioning LV. All of these elements result in the loss of the ZC and subsequent MR. This is illustrated in Figure 10.5. The downsizing and overcorrecting complete ring MV annuloplasty also has some effect on the angle and the distance of dearranged subvalvular MV apparatus by indirectly providing more leaflet tissue for ZC and by directly influencing the reduced septal-lateral diameter at the level of papillary muscle through the continuum of papillary muscle–LV wall complex.

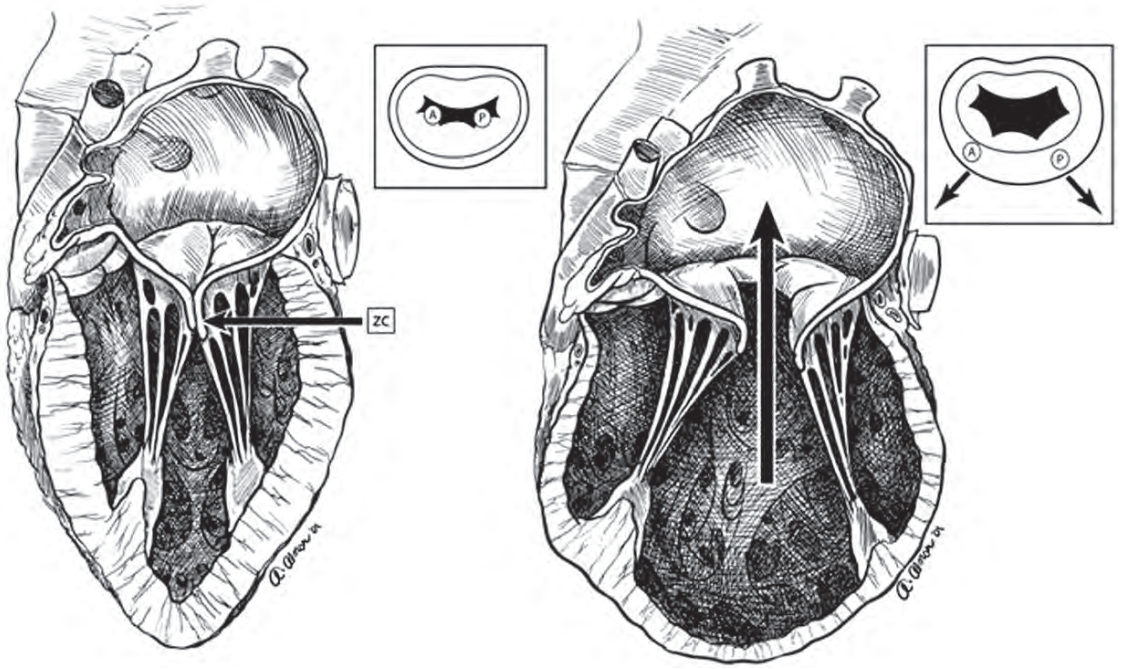


FIGURE 10.5. In nonischemic cardiomyopathy, note the geometric changes that occur from the normal to the failing LV. With the ventricular and annular dilatation of heart failure, the mitral leaflets cannot adequately cover the enlarged mitral orifice, resulting in the loss of the zone of coaptation (ZC). Geometric mitral regurgitation results from a combination of annular dilatation, papillary muscle displacement, increased leaflet tethering forces, and weakened leaflet closing forces.

Although significant undersizing of a complete ring MV annuloplasty is performed to increase coaptation, no systolic anterior motion (SAM) of the anterior leaflet, or mitral stenosis was noted in our series. SAM is not usually seen in the setting of a large aorto-mitral angle and increased LV size, both conditions that are seen in DCM.

In contrast to primary or anatomic MR, geometric MR is also reported to have dilatation along the anterior aspect of the annulus.[39] This could possibly explain why the partial ring MV annuloplasty rather than the complete ring MV annnuloplasty appears unlikely to produce a sustained long-term result.[40]

With ischemic DCM, geometric MR is furthermore compounded by the dynamic and regional changes of LV muscle function and geometry. Ischemic papillary muscle dysfunction, which is traditionally defined as the cause of geometric MR, is not merely an isolated disorder of the contractive function of the papillary muscle but a disturbance in the coordinated entire geometry of MV complex including the annulus, chordae tendinae, papillary muscles, and the LV wall. It is reported that MR cannot be reproduced by direct damage causing fibrosis of papillary muscle and it may actually decrease with papillary muscle ischemia.[41,42] This is why "papillary muscle–LV wall dislocation" rather than "ischemic papillary muscle dysfunction" has been more recently used to describe this condition.[43]

10.2.2. Geometric Mitral Valve Repair

10.2.2.1. University of Michigan Experience

In 1993, we began to use our MV repair techniques very cautiously to selected DCM patients with severe MR who were suffering from progressive severe heart failure and were not eligible for transplantation, on the assumption that the MV is the geometric functional component of the LV and that geometric MR, in which the MV apparatus itself is originally normal, is the functional and geometric problem of the LV.[17]

In 1995, a small initial series of patients at the University of Michigan was reported describing the early outcome (1993–1994) of MV repair in 16 consecutive patients with DCM and severe MR, refractory to maximum medical therapy. In this study, 16 patients (11 men and 5 women) ranged in age 44–78 years (64 ± 8 years) underwent MV repair with a simple, undersized, flexible, complete ring annuloplasty. The EF was 9–25% (16 ± 5%). Two patients were listed for transplantation. No postoperative patients required support with an intraaortic balloon pump. There were no operative or hospital deaths and mean hospital stay was 10 days. There were three late deaths at 2, 6, and 7 months after procedure, and the 1-year actuarial survival rate was 75%. At a mean follow-up of 8 months, all remaining patients were in New York Heart Association (NYHA) class I or II, with a mean postoperative EF of 25 ± 10%.[17]

Historically, while significance of MR in CHF was recognized and attempts were made to treat this surgically with MV replacement, early surgical correction was associated with poor outcomes and surgical teaching evolved to enforce this idea.[44–47] Consequently, these patients were not considered operative candidates due to the prohibitively high morbidity and mortality in this patient population.[48–52] The prevailing surgical thought was that MR provided a "pop-off" effect for these impaired ventricles to function and that by removing the MR and the "pop-off" effect the LV was compromised, which led to the high operative mortality. However, the poor outcomes of MV replacement in that era were probably from the adverse consequences of the excision and the disruption of the annular-chordal-papillary muscle continuity, which has significant importance on LV systolic function.[11,53–56] It has been demonstrated in a number of studies that preservation of the annulus-papillary muscle continuity is of paramount importance to preserve LV function, and this is even more critical in patients with severely compromised LV function.[12,57–62] Preservation of the MV apparatus and LV in MV repair has been demonstrated to enhance and maintain LV function and geometry with an associated decrease in wall stress.[63] This procedure in degenerative valvular MR has been shown to be safe, with a significant decrease in operative morbidity and mortality, and good long-term outcomes.[64–69] This supports there is no "pop-off" effect. Even though the total resistance to the LV is increased by eliminating MR, the total workload to produce the same forward flow without MR is proportionally decreased to the decreased LV volume load.[70,71]

Feasibility of the surgical treatment of geometric MR with DCM had been established by the use of the simple, undersized, flexible complete ring annuloplasty. Pre- and postechocardiography data showed some changes in parameters related

DropBooks

to hemodynamic and geometric improvement. The basal angulation of the heart was changed by undersizing, overcorrecting the annulus, and the elliptical shape of the heart became reestablished such that not only was MR acutely obliterated but the cardiac geometry was also influenced, allowing the subsequent reverse remodeling.[17–20] Figure 10.6 schematically shows how this concept might work. Encouraged by these results, we continued to apply this approach to this high-risk patient population as a first-line treatment option of heart failure.

At the University of Michigan (1993–2003), more recently 215 patients with end-stage cardiomyopathy and refractory MR underwent MV repair with a simple, undersized, complete ring annuloplasty. The range in age was 30–87 years (64 ± 12 years). EF was 6–30% (20.8 ± 6%). Preoperative NYHA class was 3.1 ± 0.9. A large number of patients (64/215, 30%) had had a previous open heart procedure. Thirty-day mortality was 4.7% (10/215) for all mitral repairs. Postoperative low cardiac output syndrome was 2.3% (5/215). Complication rates were low with cerebrovascular accident or transient ischemic attack, 2% (4/215); prolonged ventilation 6% (14/215); total infection 5% (11/215); renal failure requiring dialysis 1% (2/215); and reoperation for bleeding 0.5% (1/215). Average ICU stay was 2.67 days and average hospital stay was 7.8 days. One- and two-year actuarial survival rates have been 80% and 70%, respectively.

10.2.2.2. Experience in Other Institutions

These techniques and principles have been adopted throughout the surgical community as the contribution of the mitral annulus, chordal structures, and LV geometry to LV function were further understood.[14,72–77]

Numerous studies, from the other major surgical institutions, of MV repair in ischemic and idiopathic DCM have also noted acceptablelow operative mortality and been successful in relieving MR in CHF patients.

Chen from Brigham and Women's Hospital published in 1998 a report of 81 patients undergoing MV surgery for MR in DCM with 11% total perioperative mortality. In this series, LV mean ejection fraction (LVEF) improved from 24% to 32% and there was an improvement in NYHA class from 3.2 to 1.6. Estimated survival in this study was 73%, 58%, and 38% at 1, 3, and 5 years, respectively.[78]

Bishay and colleagues in Cleveland Clinic Foundation reported in 2000 on 44 patients with isolated MV surgery with LVEF below 35% with a 2.3%

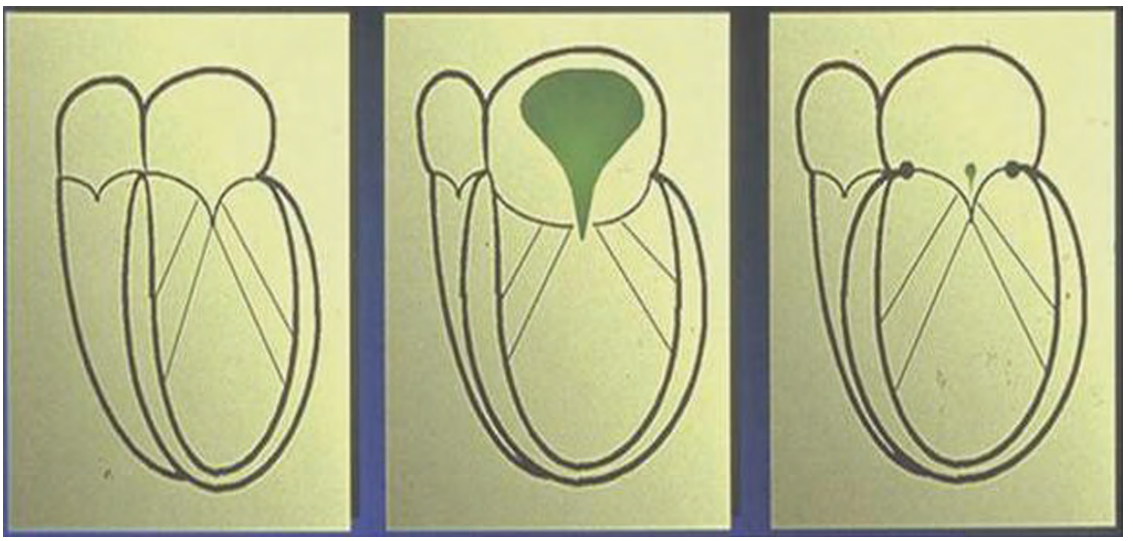


FIGURE 10.6. Geometric mitral valve (MV) repair for heart failure. Successful augmentation of the zone of coaptation (ZC) and prevention of recurrent MR can be achieved with placement of an undersized circumferential annuloplasty ring performed with multiple annular sutures. Note the changes in the relationship of the papillary muscles in the left ventricle (LV) in the new geometry following MV repair.

mortality. In this series, LVEF improved from 28% to 36% and NYHA functional class decreased from 2.8 to 1.2. Survival was 89%, 86%, and 67% at 1, 2, and 5 years, respectively. Furthermore, they noted a decrease in the LV chamber sphericity.[79]

Bitran in Israel reported in 2001 a decrease in heart failure symptoms and a decrease in NYHA functional class without any operative mortality in 21 patients with LVEF below 25%.[80]

Rothenburger from Germany in 2002 described 31 patients with isolated MV surgery with LVEF below 30% with 6.5% mortality. In this series, LVEF improved from 23% to 36% and NYHA functional class decreased from 3.3 to 2.1. Survival was 91%, 84%, and 77% at 1, 2, and 5 years, respectively. Freedom from readmission for heart failure was 85, 79, and 68% at 1, 2, and 5 years, respectively.[81]

More recently, Calafiore and associates in Italy published in 2004 a series of MV repairs in 91 DCM patients (64 ischemic and 27 idiopathic). In this study, MV annuloplasty was performed in 64 patients and 27 underwent MV replacement. The 30-day mortality rate was 4.4%. LVEF improved from 27% to 32% and NYHA functional class improved from 3.5 to 2.1 in the 69 survivors. Interestingly, the probability of being alive at 5 years was 78% and was higher in the MV repair group (81%) than in the MV replacement group (67%). The probability of being alive at 5 years with an improvement of at least one NYHA class was 66% and was higher in the MV repair group (77%) than in the MV replacement group (52%). Published series have come from numerous other units and countries and now constitute hundreds of cases performed with less than 5% mortality.[82]

The Acorn passive ventricular restraint device has also been studied in this group of patients. In the most recent Acorn series, a prospective, randomized and controlled, multi-institutional, multisurgeon experience in 193 patients with MR and a mean EF of 23.9%, LV end-diastolic dimension 69.7 mm, in which most of them underwent undersizing geometric MV repair, showed that MV surgery in DCM patients with MR could be performed with a 1.6% 30-day mortality. One- and two-year survival rate was 86.5% and 85%, respectively. This Acorn trial is also a unique opportunity to assess the long-term efficacy of MV surgery in patients with heart failure. In this report, surgery patients had a significant increase in 6 min walk times immediately after surgery and were associated with significant improvements in two different QOL measures. Surgery patients were also associated with a remarkable reversal of LV remodeling, as manifested by a decrease in LV end-diastolic and end-systolic volume, an improvement in LVEF and sphericity index, and a reduction in LV mass. MR was effectively reduced and maintained for at least 18 months of follow-up.[83] However, the Acorn cardiac support device (CSD) has not been approved by the Food and Drug Association (FDA), because the material used to make the device makes further surgery very difficult if it is a transplant and impossible if the native heart is to be preserved.

Many lessons have been learned in these geometric MR patients and further understanding and advances continue to be published in clinical and basic studies. The anterior trigone to trigone distance does enlarge in this type of CHF patient and it is not a good or useful guide for ring sizing. Anatomic and laboratory studies have confirmed this dilation of the anterior trigone to trigone distance from ischemia and DCM.[39,84,85]

It has recently been reported that partial ring annuloplasty, not complete ring annnuloplasty, is more likely to fail requiring repeat intervention.[84] Furthermore, undersizing or downsizing has been shown to be helpful not only in abolishing MR but also in remodeling the base of the heart from the "bending" of the mitral annulus. This geometric rearranging may have helped reestablish an ellipsoid shape to the base of the LV cavity. However, it should be noted that there is also emerging evidence that despite good early results, undersized annuloplasty does not serve all patients well in the short or intermediate term.

Based on the continually evolving understanding of this complex disease process and clinical experience, geometric MV repair by using the simple, undersized, overcorrected, complete ring annuloplasty is safe and effective for improving both symptoms and heart function in the short-term. However, the durability and survival benefit of this procedure is still open to question. It should be underscored that symptom reduction, reduced hospitalization, and improvement in QOL should be the treatment targets for these patients in heart failure.

Figure 10.7 shows the different types of rings commonly used to repair MR.

DropBooks

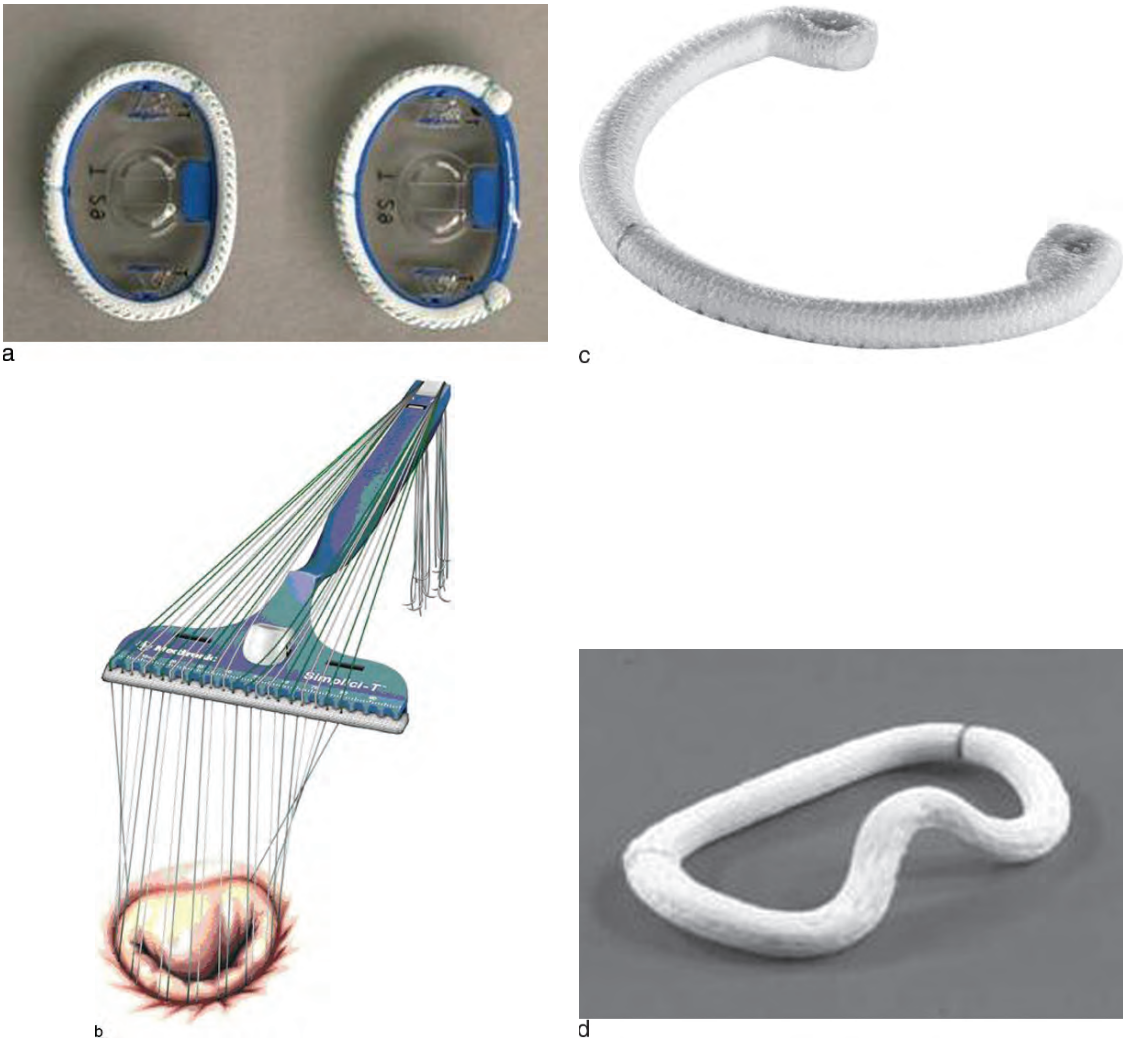


FIGURE 10.7. Range of rings available. **a** Flexible Rings. The Duran Ring which is flexible, and can be partial or complete. **b** The flexible Simplicit band. Rigid Rings. **c** Semi-rigid Band—CG band. **d** GeoForm Ring. Oblique view of the GeoForm (Edwards Lifesciences) mitral annuloplasty ring. Note the posterior ring design element which reverses the adverse changes in the posterior mitral annulus associated with geometric mitral regurgitation.

10.2.2.3. Unresolved Issues, Future Perspective

Despite these new insights, residual or recurrent MR and, more importantly, limited LV reverse geometric remodeling have also been noted and potentially limit long-term improvement.[86–88] LV remodeling is characterized by progressive LV dilatation with a change in the heart from an ellipse to a more spherical shape and is one of the strongest predictors of mortality in heart failure patients. Despite optimal surgical and/or medical therapy, heart failure is often progressive without reversal of LV remodeling. Surgical CHF treatment must, therefore, be aimed not only at MR but, more importantly, also at LV reverse remodeling.[89,90]

In a recent retrospective analysis from our institution, the effect of MV repair was compared with medical therapy in heart failure patients with severe MR. Wu et al. examined 293 patients treated medically and 126 treated with MV repair, all with severe CHF, and found that MV repair

did not predict a mortality benefit.[91] In this nonrandomized, but propensity-matched series, the results showed qualitative improvement, but there appeared to be little mortality benefit of MV repair for geometric MR in advanced heart failure and severe LV dysfunction over the 10-year period of the review. Indeed, the only predictor of mortality in this study, as in every CHF trial, medical or surgical, was reverse remodeling, which did not correlate well with the abolishment of MR. CHF-associated MR from LV geometric distortion does not preclude successful MV repair. However, it may be inferred that reducing MR in these patients may not be "enough," as MR is a late marker for CHF.[92,93] Interestingly, with further analysis of the same data set, there is favorable trend upon mortality, during the last 5 years of the study, when MV repair evolved to include earlier surgical referral for CHF patients, and the use of rigid smaller, remodeling rings. Similarly, the recently presented Acorn trial results also showed QOL benefit, but did not have a mortality benefit.

In this setting, when recurrent MR might prove to be the final pathway by which a patient decompensates, it might be worthwhile considering alternatives such as MV replacement with complete preservation of chordal supports.

Editor's Note: In our experience at The University of Chicago, we have found a group of patients with bad ventricles, especially with very tethered posterior leaflets or very large ventricles, to have suboptimal long-term results with tight mitral annuloplasty alone. In these patients, either as a first procedure or at redo surgery, we prefer to reconstruct the MV with a chord preserving prosthetic MV replacement.

Young patients tend to get mechanical MV prosthesis as shown in Figure 10.8.

Older patients (over the age of 60–65 years) usually get a porcine bioprosthetic valve with chordal preservation. This is shown in Figure 10.9.

In a recent review from the University of Michigan, we also looked at the outcome in 289 patients with EF ≤ 30%, who received an undersized complete mitral ring as their geometric MV repair procedure. Of these, 170 patients had a flexible ring. In follow-up, 16 "flexible" patients (9.5%) required a repeat procedure for significant recurrent geometric MR and CHF (10 replacements, 3 rerepairs, and 3 transplants). In contrast, 119 patients

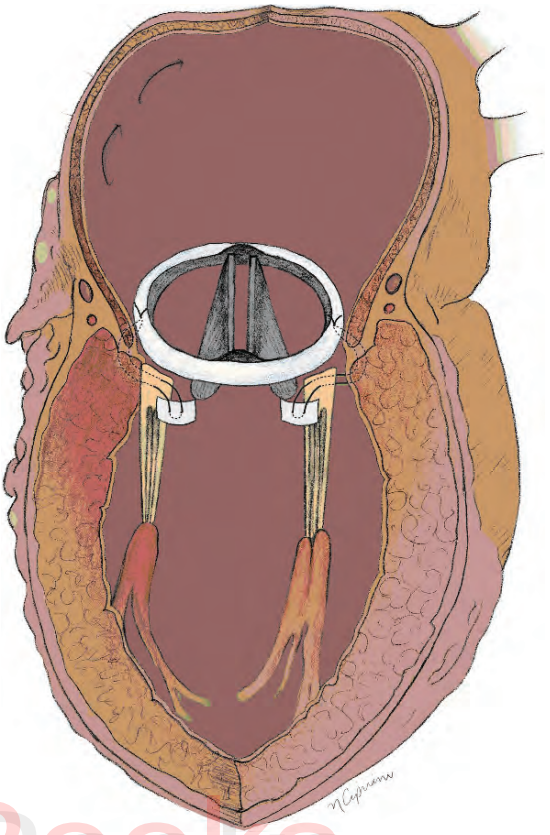


FIGURE 10.8. Mitral valve replacement with a mechanical prosthetic valve, with preservation of chordal supports. This technique is suitable in younger patients.

DropBooks

with an EF ≤ 30% received an undersized nonflexible complete ring. Only one "nonflexible" patient required a repeat MV procedure for recurrent MR secondary to ongoing ventricular remodeling and two patients required a heart transplant (2.5%). A significant difference in reoperation rates, for recurrent MR, between the groups was noted at $p = 0.012$. There were no differences between groups, in terms of age, ring size, preoperative EF, LV size, MR grade, or NYHA class.[40] From this study, it is concluded that the use of a flexible ring appeared to be associated with an increased incidence of recurrent MR and deserves further investigation through a randomized trial.

Recent developments in MV repair have included newer rings aimed at three-dimensional modulation of LV geometry through an annular approach.[94] The

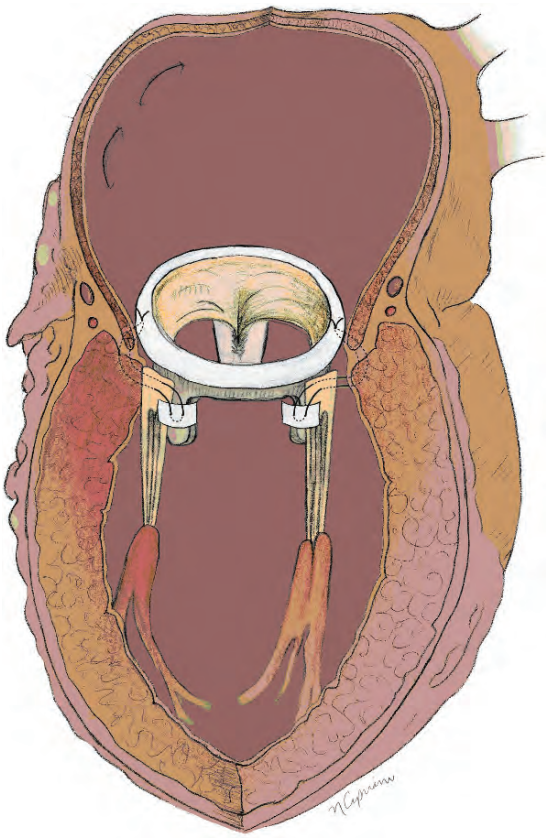


FIGURE 10.9. Mitral valve replacement with a porcine bioprosthetic valve with maintenance of chordal supports. This technique is suitable in older patients and patients with limited life expectancy.

GeoForm ring (Edwards Lifesciences, Irvine, CA) is a unique nondeformable titanium three-dimensional device aimed not only at abolishing MR but also at acutely initiating reverse LV geometric remodeling and was developed by Dr Bolling and Dr Alfieri. The anteroposterior (AP) or septal-lateral diameter is 40% reduced compared with standard ring dimensions. This AP reduction has been shown in mathematical computational modeling and in animal studies to dramatically abolish MR. This reduction in AP diameter was more effective than a reduction at P1 or P3 areas of the mitral annulus, even for "asymmetric" MR. While the GeoForm is reduced in AP diameter, the effective orifice area (EOA) of the ring is correspondingly bigger than a same size standard ring, due to the complex three-dimensional orientation of the orifice and mitral stenosis has not been seen.



FIGURE 10.10. Superior view of the GeoForm (Edwards Lifesciences) mitral annuloplasty ring. The three-dimensional cross-sectional area is not restrictive to atrial blood flow.

The three-dimensional nature of the GeoForm is directed to altering the geometry of LV. Based on the double toroid or saddle shape of the normal MV during systole, the mid-posterior ring is elevated 6 mm superior and drawn 5 mm anteriorly. Figure 10.10 shows the shape of the ring. From the surgeons' viewpoint, this shape in essence "moves" the LV and mitral annulus upward and forward as a whole to the normal position, directly reversing the trend of the CHF ventricle to "fall" down and outward. Although coronary alteration is a theoretical concern of this shape, there has been no circumflex bending or resultant ischemia in any implant, animal or human. Additionally, chordal tensioning studies, both by computer modeling and in pulse duplicators, actually demonstrated less chordal tension after GeoForm implant, which corrects LV geometry, than in the original state of a large myopathic, round heart. There has not been any chordal rupture following GeoForm implant. The three-dimensional echocardiographic picture in Figure 10.11 shows the ring maintaining the saddle shape of the annulus.

Between January and November 2004, in this initial feasibility series, 10 consecutive, nonrandomized CHF patients at the University of Michigan Medical Center, with ischemic or nonischemic DCM and refractory moderately-severe or severe MR, were studied prospectively. Patient ages ranged from 53 to 79 years (mean 73 ± 6 years). Five patients had nonischemic DCM, while five had ischemic disease. No patient was felt to have an acute myopathy. Preoperatively, six patients had NYHA class IV CHF and four had class II–III. The mean duration of documented cardiomyopathy or

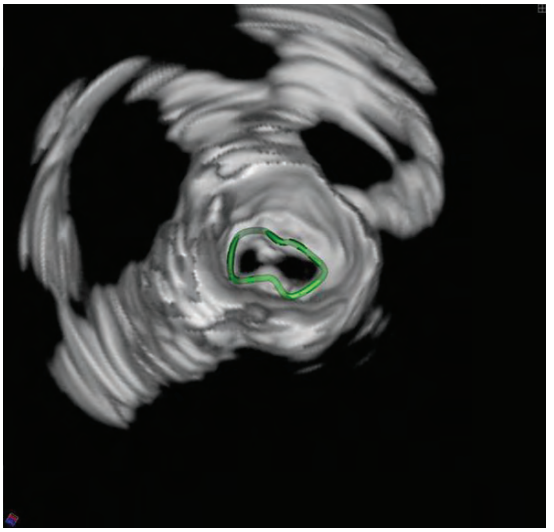


FIGURE 10.11. Postoperative three-dimensional echocardiography of a mitral repair performed using the GeoForm (Edwards Lifesciences) mitral annuloplasty ring. Note the apposition of the central areas of the anterior and posterior mitral valve (MV) leaflets which help to establish a zone of coaptation (ZC) and abolishing mitral regurgitation.

symptomatic CHF was 4 ± 6 years. Mean preoperative EF was 27 ± 11 (6–41%).

At the time of surgery, patients underwent MV repair with a GeoForm remodeling annuloplasty ring. Coronary artery bypass grafts (mean 2.9) were placed in five patients with coronary artery disease. Additional procedures included tricuspid valve annuloplasty in seven patients, atrial septal defect (ASD) or patent foramen ovale (PFO) closure in four patients, and modified Maze procedure in four patients, where indicated. There were no operative deaths.

There were no in-hospital deaths and the mean duration of hospitalization following surgery was 5.2 days (range 4–23 days). Follow-up was available for all patients. At a mean follow-up of 5 months, all surviving patients are in NYHA class I or II. The NYHA class significantly fell for every patient individually from a mean of 3.2 ± 0.4 to 1.4 ± 0.4 for the entire group.

Follow-up echocardiography at 1 week and at 3 and 6 months was obtained in all patients. The mean transmitral gradient on follow-up at 1 week was 3 ± 1 (range 1–5) mmHg. All patients had a marked reduction in sphericity, regurgitant volume, and regurgitant fraction, and significantly improved LV EF, end-diastolic volume, and end-systolic volume. There have been two late deaths, following GeoForm MV repair. One late death occurred as a consequence of recurrent acute respiratory distress syndrome (ARDS) (extra corporeal membrane oxygenation (ECMO) (supported patient, EF = 6%) and CHF at 5 months and the other was from acute sudden death at 11 months, while watching television.

Interestingly, these GeoForm patients not only demonstrated immediate clinical improvement but also showed acute favorable changes in LV geometry as shown by echo at 5 days post-op; decreased LV volumes, sphericity, and tenting height with an increase in EF, as opposed to the expected drop in EF when MR is corrected. These types of changes are not dependent on volume loading and are not usually seen acutely with echos following the use of standard rings. These beneficial changes demonstrate potential acute reverse remodeling because of the three–dimensional-shaped GeoForm ring in addition to the slow and chronic reverse remodeling. This favorable trend also appeared to be sustained in these high-risk geometric MR patients in short-term early observation (Figure 10.12).

The GeoForm ring appears to not only improve MR but, far more importantly also reverses the LV remodeling acutely and chronically associated with CHF. Larger series with longer follow-up will be needed to confirm this novel approach.

Editor's Note: While this is an exciting new ring and shows early promise, we have had at least one instance of mitral stenosis and one of mitral ring dehiscence with this ring placed in other institutions. As with all rigid structures trying to constrain a dynamic mitral annulus, there may be excessive tension on the implanting sutures. Despite all the theoretical benefits of septal-lateral cinching of the mitral annulus in animal models, it must be remembered that addressing the annulus alone in patients where the abnormality is in the underlying ventricle may be a solution doomed to failure.

10.2.3. Patient Selection for Geometric MV Repair

Based on our clinical experience, the relative contraindications to MV operations include right ventricular

DropoBooks

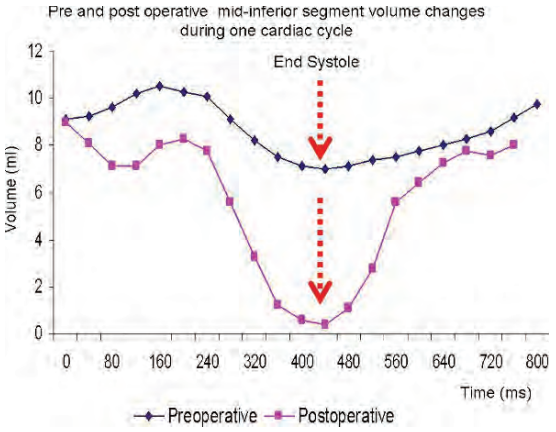


FIGURE 10.12. LV volume changes obtained on postoperative day 5 following geometric mitral valve (MV) repair. Increases in regional ejection fraction (EF) in the inferobasal wall are shown, which is the opposite of the decreased EF expected following mitral valve replacement based on historical teaching. Courtesy of Nadia Nathan, MD.

failure, severely enlarged LV diameter and volumes, elevated pulmonary artery pressures, and extremely high norepinephrine levels, tumor necrosis factor (TNF), and brain natriuretic peptide (BNP). All of these are markers of long-term end-stage CHF. These were all absolute contraindications early on in our series but we have since relaxed these considerably over time as our experience has grown and newer surgical techniques and patient management strategies have evolved.

Exact patient selection criteria remain to be elucidated, but these criteria must be considered when evaluating high-risk patients for MV repair. It is important to follow these patients closely after their procedures as the role of careful medical management of their heart failure should be emphasized.

It is important to decide which patients would benefit from MV repair and which patients are likely to fail with a MV ring annular approach. A recent presentation by Dr Alfieri's group suggested that the factors associated with positive outcomes in geometric MV repair in DCM were presence of reverse remodeling (>15% reduction in LV end-systolic volume), resolution of inferior wall ischemia, and successful ablation of atrial fibrillation. Conversely, patients without these features tended to have a poor outcome with MV repair.

Therefore, in this group of patients, it is important to conduct a study comparing MV repair using a small ring and a MV replacement with total chordal preservation.

10.2.4. Other Innovative Options to Approach Geometric MR

There are many other innovative surgical and interventional options to approach geometric MR that have been emerging and evolving, including scar resection with papillary muscle reimplantation,[95] intraventricular papillary muscle imbrication,[96] external infarct LV wall plication,[97] chordal cutting,[98] papillary muscle sling,[99] papillary muscle relocation,[100] BACE, Myocor, Myosplint, Coapsys: external bands buttressing device,[101] localized epicardial balloon patch,[102] percutaneous annular reduction by coronary sinus compression,[103] and percutaneous intraluminal edge to edge repair by using clip.[104] Most of these are still in experimental phase. Some are in preliminary clinical trial or small clinical series. The effectiveness, safety, and durability of these techniques remain to be studied.

10.3. Summary

Considering the increasing incidence and growing population of patients with CHF, there remains a need for effective medical treatment options, and also effective nontransplant, nonmechanical circulatory support device surgical treatment options. In an effort to solve these problems, many alternative surgical and interventional strategies to treat heart failure have been emerging and evolving. Geometric MV repair is one of these important treatment options and the growing experience with this technique has evolved to the point that the current excellent results need to be tested by a prospective randomized clinical trial.[92] The procedure is safe with operative mortality rates of under 5% reported from most of the major institutions in the world. The most recent Acorn study which included multiinstitution and multisurgeon results reported an operative mortality rate of only 1.6% for MV surgery including valve replacement with nonischemic DCM patients.[83] This study also showed that MV surgery was associated with an immediate improvement

of QOL and a chronic reversal of LV remodeling. In addition to the benefits of eradicating MR, potential benefits of this conventional surgical therapy, that is, the benefits of reverse LV remodeling, should be extended to the other patient subgroups not previously considered for surgical intervention. Findings of a future prospective randomized control studies could make this new therapeutic option available to millions of patients who suffer from MR and CHF. However, it must be remembered that geometric and ischemic mitral regurgitation are due to dysfunction of the ventricle and not just the annulus. Hence the most effective solutions will probably need to incorporate ventricular components while maintaining valvular integrity.

Key Points to Remember

- Mitral valve repair or replacement in the setting of poor left ventricular function is a relatively new concept.
- This may be an effective non-transplant option in selected patients with heart failure and severe mitral regurgitation.
- Remodeling and undersized annuloplasty along with geometric mitral valve repair are promising surgical therapies that can be achieved with low operative mortality.
- Mitral valve replacement with complete chordal preservation may be another strategy that works well to address mitral regurgitation in a high risk population.
- These strategies make most sense for functional and ischemic mitral regurgitation which are essentially due to dysfunction of the ventricular myocardium, and not the annulus.

BrosBooks

References

1. American Heart Association. *Heart Disease and Stroke Statistics—2005 Update*. Dallas, TX: American Heart Association; 2005.
2. Tavazzi L. Epidemiology of dilated cardiomyopathy: A still undetermined entity. *Eur Heart J*. 1997;18(1):4-6.
3. Ho KK, Anderson KM, Kannel WB, Grossman W, Levy D. Survival after the onset of congestive heart failure in Framingham Heart Study subjects. *Circulation*. 1993;88(1):107-115.
4. Khand A, Gemmel I, Clark AL, Cleland JG. Is the prognosis of heart failure improving? *J Am Coll Cardiol*. 2000;36(7):2284-2286.
5. Levy D, Kenchaiah S, Larson MG, et al. Long-term trends in the incidence of and survival with heart failure. *N Engl J Med*. 2002;347(18):1397-1402.
6. Shahar E, Lee S, Kim J, Duval S, Barber C, Luepker RV. Hospitalized heart failure: Rates and long-term mortality. *J Card Fail*. 2004;10(5):374-379.
7. Stewart S, MacIntyre K, Hole DJ, Capewell S, McMurray JJ. More 'malignant' than cancer? Five-year survival following a first admission for heart failure. *Eur J Heart Fail*. 2001;3(3):315-322.
8. Boltwood CM, Tei C, Wong M, Shah PM. Quantitative echocardiography of the mitral complex in dilated cardiomyopathy: The mechanism of functional mitral regurgitation. *Circulation*. 1983;68(3):498-508.
9. Izumi S, Miyatake K, Beppu S, et al. Mechanism of mitral regurgitation in patients with myocardial infarction: A study using real-time two-dimensional Doppler flow imaging and echocardiography. *Circulation*. 1987;76(4):777-785.
10. Perloff JK, Roberts WC. The mitral apparatus. Functional anatomy of mitral regurgitation. *Circulation*. 1972;46(2):227-239.
11. Lillehei CW, Levy MJ, Bonnabeau RC, Jr. Mitral valve replacement with preservation of papillary muscles and chordae tendineae. *J Thorac Cardiovasc Surg*. 1964;47:532-543.
12. Sarris GE, Cahill PD, Hansen DE, Derby GC, Miller DC. Restoration of left ventricular systolic performance after reattachment of the mitral chordae tendineae. The importance of valvular-ventricular interaction. *J Thorac Cardiovasc Surg*. 1988;95(6):969-979.
13. Yun KL, Sintek CF, Miller DC, et al. Randomized trial comparing partial versus complete chordal-sparing mitral valve replacement: Effects on left ventricular volume and function. *J Thorac Cardiovasc Surg*. 2002;123(4):707-714.
14. Rodriguez F, Langer F, Harrington KB, et al. Importance of mitral valve second-order chordae for left ventricular geometry, wall thickening mechanics, and global systolic function. *Circulation*. 2004;110(11, suppl 1):II115-II122.
15. Enriquez-Sarano M. Timing of mitral valve surgery. *Heart*. 2002;87(1):79-85.
16. Carpentier A. Cardiac valve surgery—The "French correction". *J Thorac Cardiovasc Surg*. 1983;86(3):323-337.
17. Bolling SF, Deeb GM, Brunsting LA, Bach DS. Early outcome of mitral valve reconstruction in patients with end-stage cardiomyopathy. *J Thorac Cardiovasc Surg*. 1995;109(4):676–682; discussion 682-673.

18. Bach DS, Bolling SF. Early improvement in congestive heart failure after correction of secondary mitral regurgitation in end-stage cardiomyopathy. *Am Heart J*. 1995;129(6):1165–1170.
19. Bach DS, Bolling SF. Improvement following correction of secondary mitral regurgitation in end-stage cardiomyopathy with mitral annuloplasty. *Am J Cardiol*. 1996;78(8):966-969.
20. Bolling SF, Pagani FD, Deeb GM, Bach DS. Intermediate-term outcome of mitral reconstruction in cardiomyopathy. *J Thorac Cardiovasc Surg*. 1998;115(2):381–386; discussion 387-388.
21. Akasaka T, Yoshida K, Hozumi T, et al. Restricted coronary flow reserve in patients with mitral regurgitation improves after mitral reconstructive surgery. *J Am Coll Cardiol*. 1998;32(7):1923-1930.
22. Flemming MA, Oral H, Rothman ED, Briesmiester K, Petrusha JA, Starling MR. Echocardiographic markers for mitral valve surgery to preserve left ventricular performance in mitral regurgitation. *Am Heart J*. 2000;140(3):476-482.
23. Starling MR, Kirsh MM, Montgomery DG, Gross MD. Impaired left ventricular contractile function in patients with long-term mitral regurgitation and normal ejection fraction. *J Am Coll Cardiol*. 1993;22(1):239-250.
24. Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Engl J Med*. 2005;352(9):875-883.
25. Otto CM. Timing of surgery in mitral regurgitation. *Heart*. 2003;89(1):100-105.
26. Conti JB, Mills RM, Jr. Mitral regurgitation and death while awaiting cardiac transplantation. *Am J Cardiol*. 1993;71(7):617-618.
27. Lamas GA, Mitchell GF, Flaker GC, et al. Clinical significance of mitral regurgitation after acute myocardial infarction. Survival and ventricular enlargement investigators. *Circulation*. 1997;96(3):827-833.
28. Trichon BH, Felker GM, Shaw LK, Cabell CH, O'Connor CM. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. *Am J Cardiol*. 2003;91(5):538-543.
29. Blondheim DS, Jacobs LE, Kotler MN, Costacurta GA, Parry WR. Dilated cardiomyopathy with mitral regurgitation: Decreased survival despite a low frequency of left ventricular thrombus. *Am Heart J*. 1991;122(3, pt 1):763-771.
30. Robbins JD, Maniar PB, Cotts W, Parker MA, Bonow RO, Gheorghiade M. Prevalence and severity of mitral regurgitation in chronic systolic heart failure. *Am J Cardiol*. 2003;91(3):360-362.
31. Grigioni F, Enriquez-Sarano M, Zehr KJ, Bailey KR, Tajik AJ. Ischemic mitral regurgitation: Long-term outcome and prognostic implications with quantitative Doppler assessment. *Circulation*. 2001;103(13):1759-1764.
32. Koelling TM, Aaronson KD, Cody RJ, Bach DS, Armstrong WF. Prognostic significance of mitral regurgitation and tricuspid regurgitation in patients with left ventricular systolic dysfunction. *Am Heart J*. 2002;144(3):524-529.
33. Ellis SG, Whitlow PL, Raymond RE, Schneider JP. Impact of mitral regurgitation on long-term survival after percutaneous coronary intervention. *Am J Cardiol*. 2002;89(3):315-318.
34. Picard MH, Davidoff R, Sleeper LA, et al. Echocardiographic predictors of survival and response to early revascularization in cardiogenic shock. *Circulation*. 2003;107(2):279-284.
35. Popovic ZB, Martin M, Fukamachi K, et al. Mitral annulus size links ventricular dilatation to functional mitral regurgitation. *J Am Soc Echocardiogr*. 2005;18(9):959-963.
36. Rosario LB, Stevenson LW, Solomon SD, Lee RT, Reimold SC. The mechanism of decrease in dynamic mitral regurgitation during heart failure treatment: Importance of reduction in the regurgitant orifice size. *J Am Coll Cardiol*. 1998;32(7):1819-1824.
37. Otsuji Y, Handschumacher MD, Schwammenthal E, et al. Insights from three-dimensional echocardiography into the mechanism of functional mitral regurgitation: Direct in vivo demonstration of altered leaflet tethering geometry. *Circulation*. 1997;96(6): 1999-2008.
38. Yiu SF, Enriquez-Sarano M, Tribouilloy C, Seward JB, Tajik AJ. Determinants of the degree of functional mitral regurgitation in patients with systolic left ventricular dysfunction: A quantitative clinical study. *Circulation*. 2000;102(12):1400-1406.
39. Hueb AC, Jatene FB, Moreira LF, Pomerantzeff PM, Kallas E, de Oliveira SA. Ventricular remodeling and mitral valve modifications in dilated cardiomyopathy: New insights from anatomic study. *J Thorac Cardiovasc Surg*. 2002;124(6):1216-1224.
40. Spoor MT, Geltz A, Bolling SF. Flexible versus nonflexible mitral valve rings for congestive heart failure: Differential durability of repair. *Circulation*. 2006;114(1, suppl):I67–I71.
41. Dent JM, Spotnitz WD, Nolan SP, Jayaweera AR, Glasheen WP, Kaul S. Mechanism of mitral leaflet excursion. *Am J Physiol*. 1995;269(6, pt 2): H2100-H2108.
42. Kaul S, Spotnitz WD, Glasheen WP, Touchstone DA. Mechanism of ischemic mitral regurgita-

tion. An experimental evaluation. *Circulation*. 1991;84(5):2167-2180.
43. Green GR, Dagum P, Glasson JR, et al. Mitral annular dilatation and papillary muscle dislocation without mitral regurgitation in sheep. *Circulation*. 1999;100(19, suppl):II95-II102.
44. Bolen JL, Alderman EL. Ventriculographic and hemodynamic features of mitral regurgitation of cardiomyopathic, rheumatic and nonrheumatic etiology. *Am J Cardiol*. 1977;39(2):177-183.
45. Merin G, Giuliani ER, Pluth JR, Wallace RB, Danielson GK. Surgery for mitral valve incompetence after myocardial infarction. *Am J Cardiol*. 1973;32(3):322-324.
46. Oury JH, Quint RA, Angell WW, Wuerflein RD. Coronary artery vein bypass grafts in patients requiring valve replacement. *Surgery*. 1972;72(6): 1037-1047.
47. Pinson CW, Cobanoglu A, Metzdorff MT, Grunkemeier GL, Kay PH, Starr A. Late surgical results for ischemic mitral regurgitation. Role of wall motion score and severity of regurgitation. *J Thorac Cardiovasc Surg*. 1984;88(5, pt 1):663-672.
48. Bonow RO, Carabello BA, Chatterjee K, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. *J Am Coll Cardiol*. 2006;48(3):e1-e148.
49. Cooper HA, Gersh BJ. Treatment of chronic mitral regurgitation. *Am Heart J*. 1998;135(6, pt 1): 925-936.
50. Fowler NO, van der Bel-Kahn JM. Indications for surgical replacement of the mitral valve with particular reference to common and uncommon causes of mitral regurgitation. *Am J Cardiol*. 1979;44(1): 148-157.
51. Gann D, Colin C, Hildner FJ, et al. Mitral valve replacement in medically unresponsive congestive heart failure due to papillary muscle dysfunction. *Circulation*. 1977;56(3, suppl):II101-II104.
52. Schlant RC. Timing of surgery for patients with nonischemic severe mitral regurgitation. *Circulation*. 1999;99(3):338–339.
53. David TE, Uden DE, Strauss HD. The importance of the mitral apparatus in left ventricular function after correction of mitral regurgitation. *Circulation*. 1983;68(3, pt 2):II76-II82.
54. Hansen DE, Cahill PD, DeCampli WM, et al. Valvular-ventricular interaction: Importance of the mitral apparatus in canine left ventricular systolic performance. *Circulation*. 1986;73(6):1310-1320.
55. Hansen DE, Sarris GE, Niczyporuk MA, Derby GC, Cahill PD, Miller DC. Physiologic role of the mitral apparatus in left ventricular regional mechanics, contraction synergy, and global systolic performance. *J Thorac Cardiovasc Surg*. 1989;97(4):521-533.
56. Rastelli GC, Kirklin JW. Hemodynamic state early after prosthetic replacement of mitral valve. *Circulation*. 1966;34(3):448-461.
57. David TE, Burns RJ, Bacchus CM, Druck MN. Mitral valve replacement for mitral regurgitation with and without preservation of chordae tendineae. *J Thorac Cardiovasc Surg*. 1984;88(5, pt 1):718-725.
58. Hennein HA, Swain JA, McIntosh CL, Bonow RO, Stone CD, Clark RE. Comparative assessment of chordal preservation versus chordal resection during mitral valve replacement. *J Thorac Cardiovasc Surg*. 1990;99(5):828–836; discussion 836-837.
59. Horskotte D, Schulte HD, Bircks W, Strauer BE. The effect of chordal preservation on late outcome after mitral valve replacement: A randomized study. *J Heart Valve Dis*. 1993;2(2):150-158.
60. Okita Y, Miki S, Kusuhara K, et al. Analysis of left ventricular motion after mitral valve replacement with a technique of preservation of all chordae tendineae. Comparison with conventional mitral valve replacement or mitral valve repair. *J Thorac Cardiovasc Surg*. 1992;104(3):786-795.
61. Pitarys CJ, 2nd, Forman MB, Panayiotou H, Hansen DE. Long-term effects of excision of the mitral apparatus on global and regional ventricular function in humans. *J Am Coll Cardiol*. 1990;15(3):557-563.
62. Rozich JD, Carabello BA, Usher BW, Kratz JM, Bell AE, Zile MR. Mitral valve replacement with and without chordal preservation in patients with chronic mitral regurgitation. Mechanisms for differences in postoperative ejection performance. *Circulation*. 1992;86(6):1718-1726.
63. Tischler MD, Cooper KA, Rowen M, LeWinter MM. Mitral valve replacement versus mitral valve repair. A Doppler and quantitative stress echocardiographic study. *Circulation*. 1994;89(1):132-137.
64. Akins CW, Hilgenberg AD, Buckley MJ, et al. Mitral valve reconstruction versus replacement for degenerative or ischemic mitral regurgitation. *Ann Thorac Surg*. 1994;58(3):668–675; discussion 675-676.
65. Carpentier A, Deloche A, Dauptain J, et al. A new reconstructive operation for correction of mitral and tricuspid insufficiency. *J Thorac Cardiovasc Surg*. 1971;61(1):1-13.

PrepBooks

66. Duran CG, Pomar JL, Revuelta JM, et al. Conservative operation for mitral insufficiency: Critical analysis supported by postoperative hemodynamic studies of 72 patients. *J Thorac Cardiovasc Surg*. 1980;79(3):326-337.
67. Enriquez-Sarano M, Schaff HV, Orszulak TA, Tajik AJ, Bailey KR, Frye RL. Valve repair improves the outcome of surgery for mitral regurgitation. A multivariate analysis. *Circulation*. 1995;91(4): 1022-1028.
68. Goldman ME, Mora F, Guarino T, Fuster V, Mindich BP. Mitral valvuloplasty is superior to valve replacement for preservation of left ventricular function: An intraoperative two-dimensional echocardiographic study. *J Am Coll Cardiol*. 1987;10(3):568-575.
69. Kay JH, Zubiate P, Mendez MA, Vanstrom N, Yokoyama T. Mitral valve repair for significant mitral insufficiency. *Am Heart J*. 1978;96(2): 253-262.
70. Gaasch WH, Zile MR. Left ventricular function after surgical correction of chronic mitral regurgitation. *Eur Heart J*. 1991;(12, suppl B):48-51.
71. Yun KL, Rayhill SC, Niczporuk MA, et al. Left ventricular mechanics and energetics in the dilated canine heart: Acute versus chronic mitral regurgitation. *J Thorac Cardiovasc Surg*. 1992;104(1):26-39.
72. Lai DT, Timek TA, Dagum P, et al. The effects of ring annuloplasty on mitral leaflet geometry during acute left ventricular ischemia. *J Thorac Cardiovasc Surg*. 2000;120(5):966-975.
73. Levine RA, Hung J, Otsuji Y, et al. Mechanistic insights into functional mitral regurgitation. *Curr Cardiol Rep*. 2002;4(2):125-129.
74. Tibayan FA, Rodriguez F, Langer F, et al. Undersized mitral annuloplasty alters left ventricular shape during acute ischemic mitral regurgitation. *Circulation*. 2004;110(11, suppl 1):II98-II102.
75. Tibayan FA, Rodriguez F, Langer F, et al. Does septal-lateral annular cinching work for chronic ischemic mitral regurgitation? *J Thorac Cardiovasc Surg*. 2004;127(3):654-663.
76. Timek TA, Lai DT, Tibayan F, et al. Septal-lateral annular cinching abolishes acute ischemic mitral regurgitation. *J Thorac Cardiovasc Surg*. 2002;123(5):881-888.
77. Yu HY, Su MY, Liao TY, Peng HH, Lin FY, Tseng WY. Functional mitral regurgitation in chronic ischemic coronary artery disease: Analysis of geometric alterations of mitral apparatus with magnetic resonance imaging. *J Thorac Cardiovasc Surg*. 2004;128(4):543-551.
78. Chen FY, Adams DH, Aranki SF, et al. Mitral valve repair in cardiomyopathy. *Circulation*. 1998;98(19, suppl):II124-II127.
79. Bishay ES, McCarthy PM, Cosgrove DM, et al. Mitral valve surgery in patients with severe left ventricular dysfunction. *Eur J Cardiothorac Surg* 2000;17(3):213-221.
80. Bitran D, Merin O, Klutstein MW, Od-Allah S, Shapira N, Silberman S. Mitral valve repair in severe ischemic cardiomyopathy. *J Card Surg*. 2001;16(1):79-82.
81. Rothenburger M, Rukosujew A, Hammel D, et al. Mitral valve surgery in patients with poor left ventricular function. *Thorac Cardiovasc Surg*. 2002;50(6):351-354.
82. Calafiore AM, Mauro MD, Gallina S, et al. Surgical treatment of mitral valve regurgitation in dilated cardiomyopathy. *Heart Surg Forum*. 2004;7(1):21-25.
83. Acker MA, Bolling S, Shemin R, et al. Mitral valve surgery in heart failure: Insights from the Acorn Clinical Trial. *J Thorac Cardiovasc Surg*. 2006;132(3):568–577, e561-e564.
84. McCarthy PM. Does the intertrigonal distance dilate? Never say never. *J Thorac Cardiovasc Surg*. 2002;124(6):1078-1079.
85. Miller DC. Ischemic mitral regurgitation redux—to repair or to replace? *J Thorac Cardiovasc Surg*. 2001;122(6):1059-1062.
86. Hung J, Papakostas L, Tahta SA, et al. Mechanism of recurrent ischemic mitral regurgitation after annuloplasty: Continued LV remodeling as a moving target. *Circulation*. 2004;110(11, suppl 1):II85-II90.
87. Matsunaga A, Tahta SA, Duran CM. Failure of reduction annuloplasty for functional ischemic mitral regurgitation. *J Heart Valve Dis*. 2004;13(3):390–397; discussion 397-398.
88. Tahta SA, Oury JH, Maxwell JM, Hiro SP, Duran CM. Outcome after mitral valve repair for functional ischemic mitral regurgitation. *J Heart Valve Dis*. 2002;11(1):11–18; discussion 18-19.
89. Bolling SF. Mitral valve reconstruction in the patient with heart failure. *Heart Fail Rev*. 2001;6(3):177-185.
90. Bolling SF. Mitral reconstruction in cardiomyopathy. *J Heart Valve Dis*. 2002;(11, suppl 1): S26-S31.
91. Wu AH, Aaronson KD, Bolling SF, Pagani FD, Welch K, Koelling TM. Impact of mitral valve annuloplasty on mortality risk in patients with mitral regurgitation and left ventricular systolic dysfunction. *J Am Coll Cardiol*. 2005;45(3):381-387.
92. Mehra MR, Griffith BP. Is mitral regurgitation a viable treatment target in heart failure? The plot just thickened. *J Am Coll Cardiol*. 2005;45(3):388-390.
93. Patel JB, Borgeson DD, Barnes ME, Rihal CS, Daly RC, Redfield MM. Mitral regurgitation in patients with advanced systolic heart failure. *J Card Fail*. 2004;10(4):285-291.

94. Bolling S, Alfieri O, Bach D. Reforming LV geometry in CHF with MR: A unique valvular solution for a ventricular problem [abstract]. In: The 86th Annual Meeting for the American Association for Thoracic Surgery; 2006.
95. Hendren WG, Nemec JJ, Lytle BW, et al. Mitral valve repair for ischemic mitral insufficiency. *Ann Thorac Surg*. 1991;52(6):1246–1251; discussion 1251-1242.
96. Menicanti L, Di Donato M, Frigiola A, et al. Ischemic mitral regurgitation: Intraventricular papillary muscle imbrication without mitral ring during left ventricular restoration. *J Thorac Cardiovasc Surg*. 2002;123(6):1041-1050.
97. Liel-Cohen N, Guerrero JL, Otsuji Y, et al. Design of a new surgical approach for ventricular remodeling to relieve ischemic mitral regurgitation: Insights from 3-dimensional echocardiography. *Circulation*. 2000;101(23):2756-2763.
98. Messas E, Guerrero JL, Handschumacher MD, et al. Chordal cutting: A new therapeutic approach for ischemic mitral regurgitation. *Circulation*. 2001;104(16):1958-1963.
99. Hvass U, Tapia M, Baron F, Pouzet B, Shafy A. Papillary muscle sling: A new functional approach to mitral repair in patients with ischemic left ventricular dysfunction and functional mitral regurgitation. *Ann Thorac Surg*. 2003;75(3): 809-811.
100. Kron IL, Green GR, Cope JT. Surgical relocation of the posterior papillary muscle in chronic ischemic mitral regurgitation. *Ann Thorac Surg*. 2002;74(2):600-601.
101. Inoue M, McCarthy PM, Popovic ZB, et al. The Coapsys device to treat functional mitral regurgitation: In vivo long-term canine study. *J Thorac Cardiovasc Surg*. 2004;127(4):1068–1076; discussion 1076-1067.
102. Hung J, Guerrero JL, Handschumacher MD, Supple G, Sullivan S, Levine RA. Reverse ventricular remodeling reduces ischemic mitral regurgitation: Echo-guided device application in the beating heart. *Circulation*. 2002;106(20):2594–2600.
103. Kaye DM, Byrne M, Alferness C, Power J. Feasibility and short-term efficacy of percutaneous mitral annular reduction for the therapy of heart failure-induced mitral regurgitation. *Circulation*. 2003;108(15):1795–1797.
104. St Goar FG, Fann JI, Komtebedde J, et al. Endovascular edge-to-edge mitral valve repair: Short-term results in a porcine model. *Circulation*. 2003;108(16):1990–1993.

DropBooks

11
Destination Therapy with Permanent Mechanical Circulatory Assist Devices

Murali Macherla and Valluvan Jeevanandam

11.1. Introduction

Effective treatment of end-stage heart disease in the emerging population of nontransplantable candidates has been a challenge. Long-standing research, combined with technological advancement in the latter half of last century, has made permanent mechanical circulatory assist devices a reality, albeit of limited time in this group of patients. Presently, congestive heart failure (CHF) is diagnosed in more than 550,000 US residents every year, adding on to the 5 million already afflicted by the disease.[2]

11.2. Genesis of Circulatory Assist Devices

The use of a left ventricular assist device was first reported by Hall et al. in 1964, with the device connected between the left atrium and the descending aorta.[3] DeBakey et al. successfully used a paracorporeal device in a cardiogenic shock patient, who survived and was discharged from the hospital after device explantation. Triggered by the success of sustaining circulation with mechanical assistance, assist devices were used in various permutations and combinations including temporary assistance, bridge to transplantation, artificial heart, and as permanent assist device.

The treatment of CHF due to left ventricular dysfunction has evolved dramatically in the past decades.[4,5] Advances in medical treatments have helped patients in all stages of heart failure, even those with New York Heart Association (NYHA) class IV symptoms.[6,7] Although transplantation is the gold standard, its availability is limited by the shortage of donors, complications of immunosuppression, infection, and chronic allograft vasculopathy.[8]

These statistics have focused attention on mechanical circulatory assist devices for longer or permanent use. Mechanical energy was utilized by the investigators in three forms:

1. Pulsatile volume displacement: Augment systolic and diastolic pressures of the heart, demonstrated by concepts such as dynamic cardiomyoplasty,[9] the Heart Booster (Abiomed Corp, Danvers, MA),[10] and Direct mechanical ventricular actuation (DMVA).[11]
2. Continuous flow: Augment circulation by draining blood from the heart and pumping it to the arterial system with enough force to maintain adequate blood pressure.
3. Counterpulsation: This method of mechanical assistance supplies energy to portions of vascular system, decreasing the workload, increasing diastolic blood flow, and increasing the cardiac output.

11.2.1. Abiomed Heart Booster Device

This is a pericardial assist device which was tested successfully in calves. Prototypes of the device were made with fiber reinforced angioflex sheets arranged like a fan (Figure 11.1). The contractile elements are a string of adjacently placed fine tubes. Inflation and deflation of these tubes provide

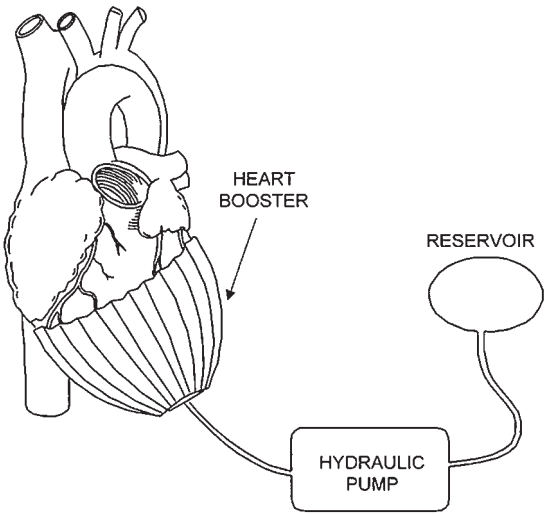


FIGURE 11.1. Heart Booster Abiomed.

systolic assistance to the heart. Negative pressure during diastole collapses the tubes completely and does not interfere with the diastolic filling. This device is wrapped around the ventricles and attached to the pericardium. Figure 11.1 shows the Abiomed Heart Booster device around the heart.

11.2.2. Direct Mechanical Ventricular Actuation

DMVA (Figure 11.2) is different from other pericardial assist devices, in the sense that the ventricular support cup is made of silicone rubber and is vacuum assisted, and pneumatically driven augmenting systole. Lack of diastolic augmentation is the pitfall in this device. Like the Abiomed Heart Booster device, this device does not come in contact with blood, thereby avoiding the complications of hemolysis, thromboembolism, etc. Implantation in bovine models has been successful.

11.2.3. Ventricular Assist Devices

Initially, it was thought that total heart replacement would be necessary, such as the Jarvik 7. The Jarvik Heart was implanted into Barney Clark, a dentist in 1982, by Dr William Devries at the University of Utah. Barney Clark lived for 112 days, with the postoperative period complicated by infections and strokes. It became clear that a vast majority of patients would benefit from implantation of ventricular assist device alone. The HeartMate/Thoratec (Thoratec Inc., Pleasanton, CA) and Novacor (WorldHeart Corporation,

DropBooks

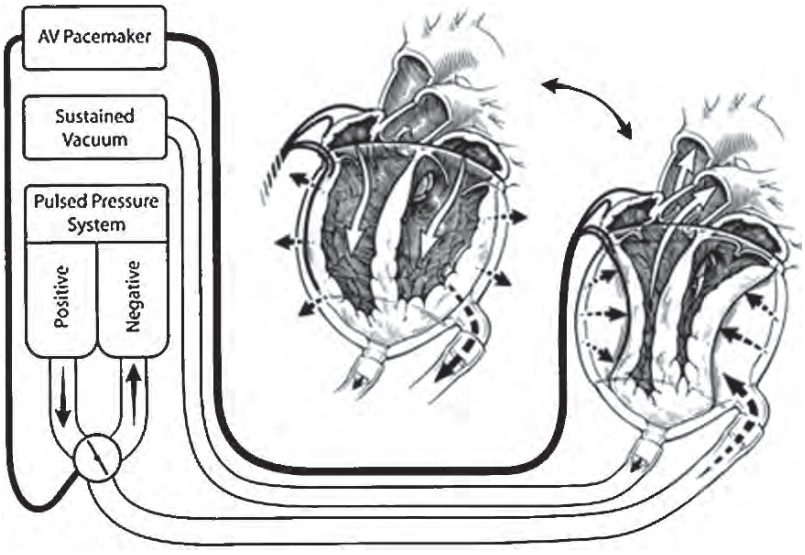


FIGURE 11.2. DMVA Anstadt cup.

Ottawa, Canada) are first-generation left ventricular assist system (LVAS) specifically developed for permanent implantation. The initial experience was in patients as a bridge to transplantation and these devices were Food and Drug Administration (FDA) approved for this indication.

Both these devices are electrically driven and have an inflow valve and an outflow porcine valve. These devices are implanted in the intraperitoneal or in the preperitoneal space, and vented to the outside. They drain blood from the left ventricular (LV) apex to the ascending aorta, or right atrium/right ventricle to pulmonary artery, depending upon the side of the heart supported. External drive lines connect the devices to controllers.

Precedence was set by the REMATCH (Randomized Evaluation of Mechanical Assistance for the treatment of Congestive Heart Failure) trial for the use of left ventricular assist device (LVAD). The HeartMate XVE was used in the REMATCH trial. One hundred and twenty-nine patients with end-stage heart failure who were not transplantable candidates were included in this study. Of this, 68 patients were randomized to receive LVAD, and 61 were randomized to optimal medical management. The patients included in both groups were all in class NYHA IV. The average age group on optimal medical management (OMM) was 68 years compared to 66 years in the LVAD group. Eighty-two percent were males in the OMM group compared to 78% in the LVAD group. One-year data demonstrated an improvement in survival from 25% to 52% in patients supported by the device in comparison to medical controls (graph-1, Survival curve). Improvement in 2-year survival was from 8% to 23%. Based on these results, the HeartMate was the first device approved for permanent implantation. Although the LVAD group showed survival advantage over OMM, they had their share of complications. The lessons learnt from LVAD placement were well outlined by Dembitsky et al.[10] They can be grouped as (a) Device-related adverse events and (b) Non–device-related adverse events. These are outlined in Tables 11.1 and 11.2.

The HeartMate device is unique in utilizing a textured blood-contacting surface. The textured polyurethane and sintered titanium spheres promote neointimal proliferation. Since the bioactive surface is nonthrombogenic, no anticoagulation is needed. The electrically actuated pusher plate design supplies energy for the pump. The housing is designed in a manner such that a random vortex is formed during each beat, leading to complete washout of blood with minimal stasis. The external components consist of two batteries and a controller weighing about 1 kg. The configuration of this device is shown in Figure 11.3.

Table 11.1. Non–device-related adverse events.

Event type	Events/patient/year
Bleeding	0.60
Neurological dysfunction	0.44
Sepsis	0.51
Local infection	0.28
Ventricular	0.23

Table 11.2. Device-related adverse events.[a]

Event type	Events/patient/year
Confirmed LVAD malfunction	0.77
Perioperative bleed	0.41
Percutaneous site/pocket infection	0.35
Pump, inflow, or outflow tract infection	0.19
LVAD-related RHF	0.16
LVAD system failure	0.10
Device thrombosis	0.04

LVAD left ventricular assist device, *RHF* right heart failure.
[a]Charts obtained from Long et al.[10]

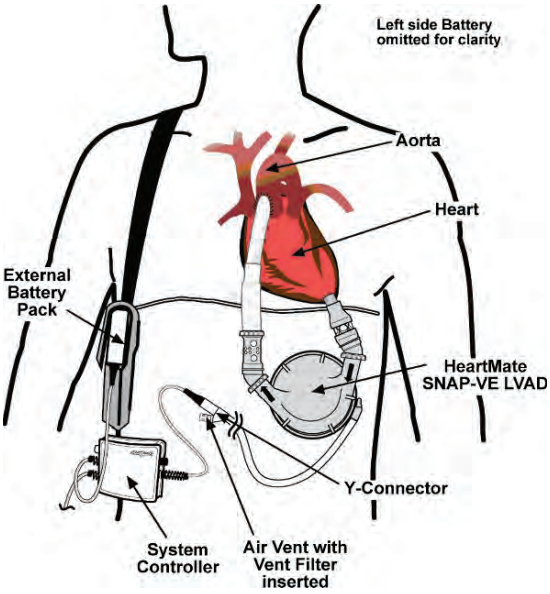


Figure 11.3. HeartMate XVE.

The advanced HeartMate model XVE LVAS (Figure 11.11) had several modifications: (1) Percutaneous lead with improved strength and occlusion resistance, (2) Vent adapter design changed to prevent breakage and make it more user-friendly, (3) Addition of locking screws on pump obviate the need for conventional sutures, (4) Outflow graft bend prevents kinking, and (5) Repositioning of the diaphragm support structure to prevent fracture of the diaphragm.[11]

The device has two modes of operation: (1) Auto mode (2) Fixed mode.

The fixed mode is volume independent and is operated at a preset fixed rate. While in the automatic mode the software in the system controller regulates the rate to the physiological demand. The rate range in both modes is 50–120 beats per minute.

Novacor LVAS (WorldHeart, Ottawa, Canada), shown in Figure 11.4, is similar to the HeartMate with regard to placement and indications for use. To date more than 1,600 devices have been implanted worldwide. This device is actuated by magnetic plates. Hence, it does not have bearings that can wear down, and stop a motor. It has proven to be more durable than the HeartMate, but requires anticoagulation, and is associated with a cerebrovascular accident (CVA) rate of 26%. Design changes have been implemented to decrease the thromboembolic rate. This is the first mechanical circulatory device which has supported a single patient for more than 6 years.

Novacor II LVAS (Figure 11.5) is in preclinical evaluations, and is a pulsatile circulatory support device. It is totally implantable, magnetically driven, with minimal wear down of parts. The inflow conduit is connected to the left ventricle of the recipient and outflow to the aorta. Its unique double-chamber design allows the system to operate without a volume compensator or a venting line through the skin. It is a smaller and quieter device than Novacor LVAS.

The RELIANT (Randomized Evaluation of the Novacor LVAS in a Non-Transplant Population) trial is in progress. The objective of the study is to show the superiority over the optimal medical treatment and its equivalence to the HeartMate LVAD.[12]

The next generation devices are of direct pumping type, and they propel blood in a nonpulsatile fashion using axial flow or centrifugal technology. The primary advantage over the earlier devices is the reduction in size. These devices are not larger than “D” size battery and do not require venting or compliance chamber. They can pump up to 10 L, depending on the afterload. Hemolysis is not an issue in properly placed devices. Developing control mechanisms to prevent “sucking” of the LV cavity has been a challenge. If devices are left at high rpm, they will empty the ventricular cavity, entrain debris into the pump, and stop. This problem was overcome by operating the pump at low rpm and not letting the ventricular cavity empty completely. These pumps, if optimally run, drain the heart and produce nonpulsatile flow. Since

DropBooks



Figure 11.4. Novacor LVAS.



Figure 11.5. Novacor II LVAS.

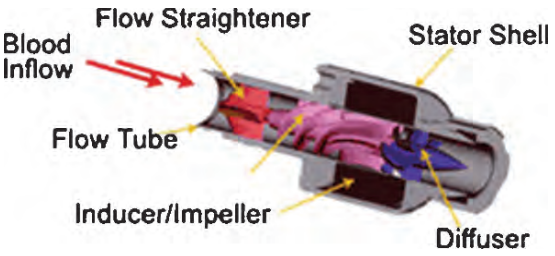


FIGURE 11.6. Micromed Debakey pump.

these pumps are run lower than the maximal flow, some degree of pulsatility is seen because of the ejection from the heart. Compared to the earlier generation LVADs, second-generation LVADs are partial unloading devices. It will be interesting to determine whether minimal pulsatile support can recover a patient from heart failure syndrome.

There are three next generation devices: (1) The Micromed DeBakey pump (Figure 11.6), (2) Jarvik 2000, and (3) HeartMate II. Each device is in various stages of bridge to transplantation and destination therapy evaluation. Preliminary results suggest that these devices can reverse heart failure. The incidence of infection is similar to that with first-generation devices. The right heart failure (RHF) and bleeding complications are also similar. These devices require heavy anticoagulation. They have bearingless, magnetically levitated rotors and should last 5–10 years.

This miniature pump developed with NASA technology measures 2.5 cm × 7.5 cm and is capable of pumping 10 L/min. The compact design makes it a suitable choice for small built individuals. The simplicity of design with one moving part, the impeller, and noiseless functioning of the device may be attractive for the patient. The disadvantage is that it requires heavy anticoagulation. The information from the company release lists about 330 devices that have been implanted worldwide.

Figure 11.7 shows the Jarvik-2000 which is a newer generation VAD that is small (about the size of "C" battery) and capable of 7 L/min flow rates. The unique design makes it totally implantable in the left ventricle. The motor is enclosed in a titanium housing. The rotor is supported by two ceramic housings and has a single moving part, which is the titanium impeller. This device can run for 8–10 h on a single portable lithium pack. About 100 devices have been implanted worldwide.

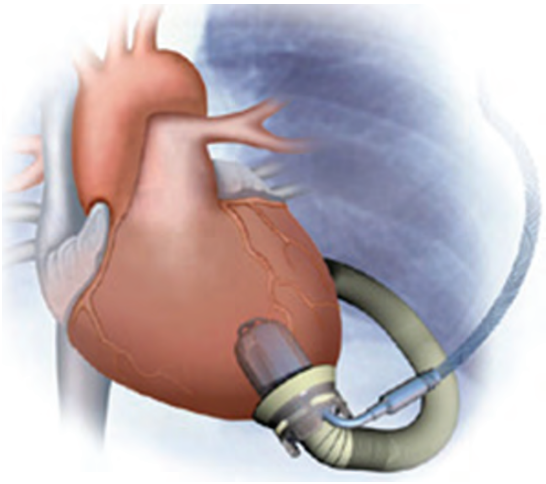


FIGURE 11.7. Jarvik 2000.

HeartMate II LVAS (Figure 11.8). This is also a compact LVAS with a single moving part. This device is capable of pumping 10 L/min. It weighs 400 g and easily implantable. Early clinical outcomes suggest low thrombosis, low hemolysis, and low infection rate. This device is silent and vibration free, adding to patient comfort. The hydrodynamic bearings are simple to operate and reliable. About 100 devices have been implanted so far.

All the VADs discussed above are "obligatory" devices. Since blood travels outside the normal path and through a motorized device, these cannot be stopped even for short period of time, without the risk of blood stasis and thromboembolic events. Second- and third-generation devices do not have valves, and regurgitation is an additional problem

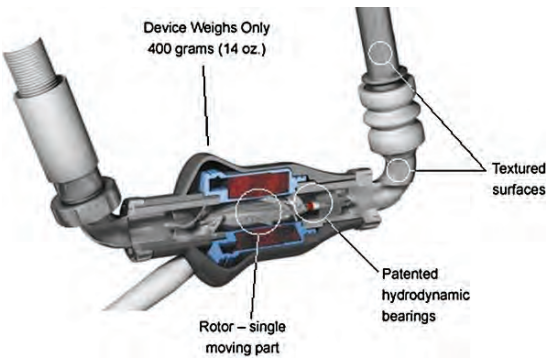


FIGURE 11.8. HeartMate-II.

if the device is stopped. Depending on the device, the regurgitant amount can vary from 1 L to 3 L. The MicroMed Debakey pump is the only device that addresses this issue by employing a balloon that inflates in the outflow graft and shuts off regurgitant blood flow.

11.2.3.1. Right Ventricular Assist Devices

Right ventricular assist devices (RVADs) can be used in combination with LVAD or alone.[13] They work effectively if implanted before irreversible end organ occurs.[14] RVADs can be placed on pump and off pump. Ten to fifteen percent of patients undergoing LVAD placement require RVAD placement. The inflow cannulae are placed in the right atrium, right ventricle, or the right ventricle outflow tract. The outflow cannula is placed directly on the main pulmonary artery. Newer techniques of cannulating the right pulmonary artery off-pump[15] in redo patients have been reported.

Concomitant use of RVAD with LVAD is associated with increased operative mortality.[17] The inability to reliably predict the early onset of RHF contributes to this problem. The best way to treat RHF is by avoidance.[18] Intraoperative and postoperative measures can be undertaken to protect right heart. These include the following:

patient selection and timing;
serine protease inhibition;
right heart myocardial protective techniques;
use of leukocyte-depleted blood products;
maintenance of perfusion and mean pressures (vasopressin);
and right heart venting or bypass.

Postoperatively aggressive treatment of acidosis; hyperventilation (hypocarbia); use of nitric oxide; AV synchrony by pacing; and early postoperative continuous veno-venous hemofiltration (CVVH) will help right heart protection.[18]

11.3. Counterpulsation

The method of mechanical assistance is used to supply energy to portions of the vascular system to decrease the workload of the heart and increase cardiac output. The original work of diastolic augmentation originated in the laboratory of Charles Wiggers in 1953. Dr Adrian Kantrowitz and colleagues began to investigate the use of a mechanical prosthesis as an auxiliary ventricle (MAV) that was placed in series with the circulatory system and could provide diastolic assistance.[19] Moulopoulous et al.[20] experimented with an intra-aortic balloon pump (IABP), as did Clauss. These were precursors of the now ubiquitous IABP. The first permanent implantable balloon also known as the CardioVAD Implantable IABP was implanted in Mr. Clifford Doyle, a 73-year-old retired policeman, on October 30, 2000, at the University of Chicago hospitals.

The concept of counterpulsation leading to improvement in myocardial function has been proven with the IABP. It is the most frequently used mechanical assist device in the world, (100,000 annually, personal communication Datascope Corp.). The IABP has been used for the treatment of Cardiogenic shock, primarily ischemic as well as postcardiotomy, myocarditis, transplant rejection, and as bridge to transplant. IABP increases coronary blood flow and decreases myocardial work marginally. It is also used in chronic heart failure patients to recover from the state of CHF by decompressing the heart and bringing the myocytes to a better portion of the starling curve.[21] The beneficial effects of the balloon pump can be long lasting after removal.

Cardiovad (KCV) is a nonobligatory device. The unique feature of this device is that the patient has a choice of turning off the assist device for minutes to hours and no anticoagulation is required. Figures 11.9 and 11.10 show the CardioVAD configuration in a patient and the mechanism of action. This device has three main parts:

1. Blood pump, which is implanted in the aorta.
2. Percutaneous access device (PAD), which is a connector and connects the blood pump to the external drive unit.
3. External drive units, which come in two models: (1) a small battery powered model that can be worn in a vest or as a shoulder bag and (2) a portable suitcase model.

Figure 11.11 is a photograph of the balloon with the stiff backing that is sutured into the aorta.

The present eligibility criteria for the CardioVAD implantation include the following:

DropBooks

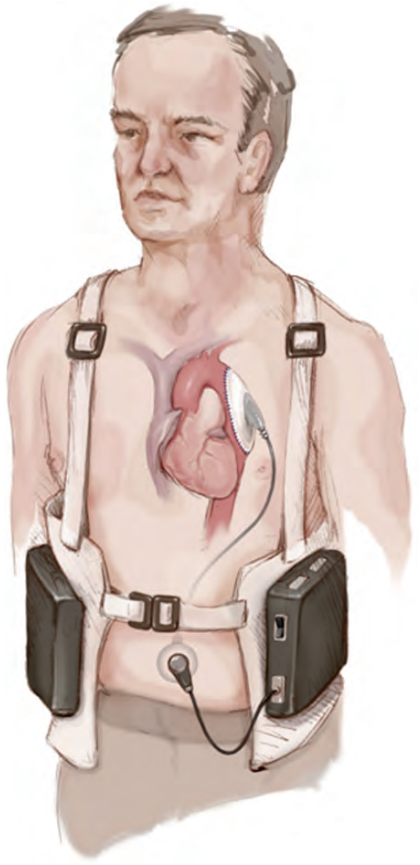


FIGURE 11.9. The Kantrowitz CardioVAD System.

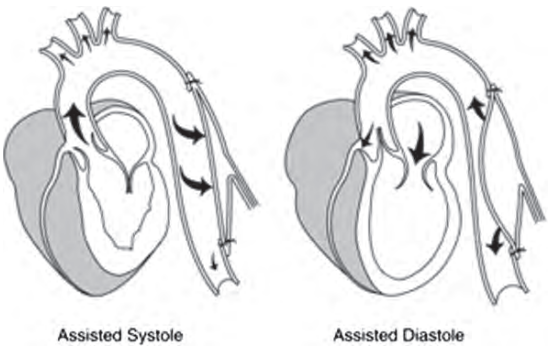


FIGURE 11.10. Assisted systole; assisted diastole.

1. 18–80 years of age (although the effect may not be significant in younger patients with compliant aortas).
2. CHF not treatable with the standard medical or surgical methods.

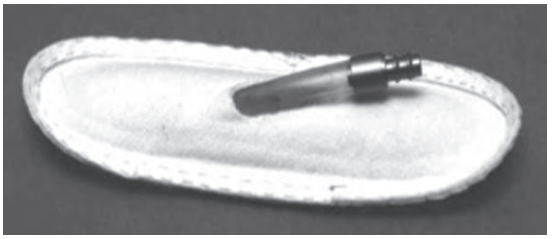


FIGURE 11.11. The advanced HeartMate model XVE LVAS.

3. Not a transplant candidate.
4. If female, are postmenopausal, surgically sterilized, or practicing an effective method of birth control.
5. Patient willing to live within 100 miles of the hospital where implantation was done.

The pump installed is in the proximal descending aorta and works by

1. increasing diastolic blood pressure and flow,
2. decreasing the afterload,
3. increasing coronary flow,
4. increasing the mean arterial blood pressure, and
5. decreasing the workload of the left ventricle.

The blood pump consists of an oblong, inflatable bladder mounted in a semi-rigid plastic shell. The bladder provides about 50–60 cc of stroke volume. This is anastomosed to the native proximal descending aorta using two rows of mattress sutures.

The PAD consists of a Dacron covered 8-cm-diameter disk that rests on the abdominal fascia. The stem made of polycarbonate traverses the skin. A unique feature of the CardioVAD that decreases the risk of infection at the PAD site is the creation of biological interface. A skin biopsy is obtained 2 weeks prior to CardioVAD placement. Fibroblasts are cultured and allowed to proliferate over the polycarbonate PAD. This biological interface prevents downward growth of the patient's epidermal layer, which can lead to marsupiliazation and creation of infection-prone sinuses.

The external drive houses the pneumatic compressor and the microprocessor to actuate the pump. These are connected to the PAD via a flexible, removable driveline. The microprocessor automatically analyses the electrical signal

from the heart and triggers the CardioVAD during diastole. The compressor shuttles pressurized room air between the console and the pump. This unit is available in two models. The suitcase model weighs 40 lb and can be moved around with moderate ease. The vest model comes in two 2.5 lb rectangular units of battery and microprocessor.

The initial feasibility trial was designed to test the device at 1 and 3 months. Nine nontransplantable patients were enrolled, of which two were bedridden. Eight male and one female patients were included in the study. All the patients included in this trial were in severe heart failure NYHA class IV and dependent on intravenous inotropes. No other treatment options were available to them. Age range was from 53 to 74. Seven of the patients were diagnosed with ischemic cardiomyopathy, of which five had previous CABG. One patient had St. Jude's aortic valve placement. The ejection fraction was 16 ± 5% (range 9–24%). The mean weight loss during the year prior to KCV implantation was 31 ± 5 lb.

Of the nine patients, surgery was abandoned in one patient because of severe pleural adhesions. One died in the operating room because of technical problems arising from left atrial to femoral bypass. In the other seven patients, the CardioVAD was implanted with the aid of cardiopulmonary bypass (CPB). All of them were extubated within 48 h and survived the first endpoint of 30 days. The mean CPB time was 157 min (range 120–196 min), and the crossclamp time was 62 min. This timing decreased to half as we gained more experience. There were no reoperations for bleeding and the mean chest tube blood loss was 450 cc (range 250–900). Postoperatively all the patients were weaned of inotropes, maintaining the end-organ perfusion. At the time of discharge all the patients were on aspirin except for the patient with mechanical aortic valve, who was discharged with coumadin. The reductions in serum creatinine, RA and PCWP, as well as increase in CI were statistically significant when compared with the baseline values. Although the quality of life parameters and the 6-min walk distance improved, the differences were not significant.

Paraplegia can be a potential complication. The intercostal arteries were not disrupted, but occluded temporarily with a Fogarty catheter, to prevent back bleeding into the surgical field. Our study showed that the Kantrowitz CardioVAD could be implanted safely, with improved hemodynamics and reversal of heart failure. Follow-up at 1 month showed reduction in PCWP, RA pressures with an increase in cardiac index. Renal function significantly improved with normalization of serum creatinine levels. There were late air embolism, causing strokes and ultimate demise of most of the patients at the 6–15-month mark. There were no hemolytic events or derangement of coagulation or liver function parameters during the 1-month period.

KCV being a nonobligatory device simplifies outpatient management. With the only on/off patient-controlled switch, this device allows patients to carry on activities of daily life without being tethered to the device. KCV had device-related problems, which required modifications. The PAD connection was made air and watertight, after desiccated particles were noted due to seepage of tissue edema fluid. The PAD stem was made longer to fit patients with this body habitus. Two patients had microscopic pinholes developed in the pump. The blood pump was redesigned and made shorter and more flexible. CardioVAD II, newest version of this device, has been implanted twice with reasonable results.

Our experience with the nonobligatory KCV showed low operative mortality and morbidity. Patients liked the freedom from anticoagulation and the simplicity of the device. However, it has some drawbacks. This device provides only partial support, and depends on some ejection by the native heart. It is not suitable for patients with impaired biventricular function, uncontrolled arrhythmias, or native valvular disease.

On the basis of a similar concept, William Peters set up Sunshine Heart in Australia and New Zealand and developed C-Pulse heart (Figure 11.12). This assist device is in clinical trial in Australia and New Zealand. The first human implant was done on May 9, 2005. This device has balloon cuff which is wrapped around the ascending aorta. The balloon pump does not contact blood and gives 20-cc augmentation. This device placement does not require CPB. The driver units are similar to CardioVAD. Although this concept is promising, it is probably limited by length, and the presence of atherosclerotic disease or bypass grafts in the ascending aorta. Since the balloon volume is low (20 cc), the amount of CHF reversal remains to be seen.

BrownBooks

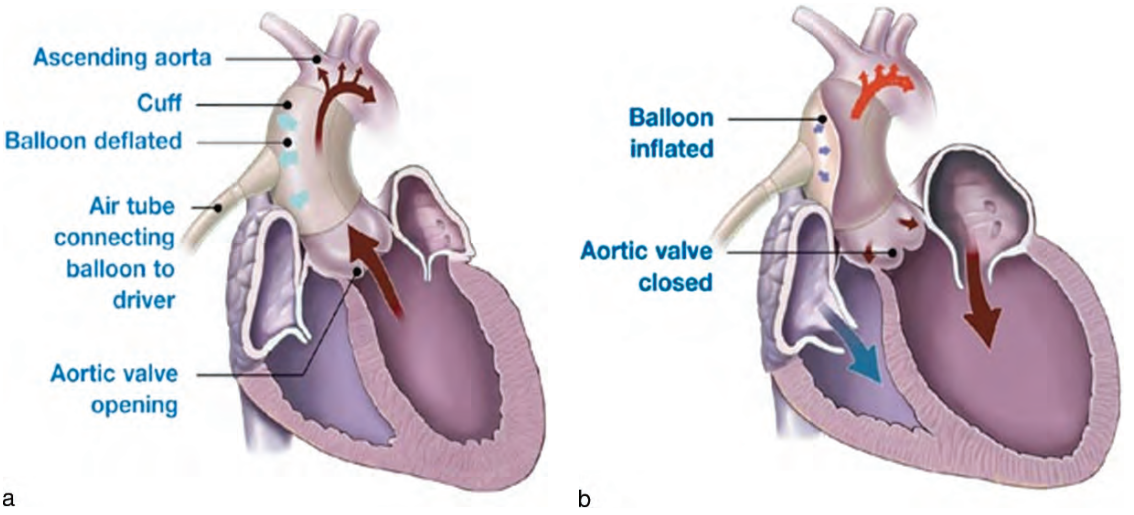


FIGURE 11.12. C-Pulse heart.

11.4. Destination Therapy

A steadily aging population has forced us to consider alternatives to transplantation such as destination therapy with VADs for end-stage heart failure. Ventricular assist devices have been in use for more than a decade. Encouraged by the improved outcomes of the REMATCH trial, investigators explored the possibility of using assist devices as destination treatment, in patients who are not transplant candidates. Only 5–15% of patients undergoing VAD placement as a bridge to transplant recover the native heart function and undergo device explantation.[16] At present, the only FDA-approved device for destination therapy is the HeartMate XVE. Two destination therapy trials are underway, that is,

1. RELIANT trial approved by FDA in 2004. This trial will be conducted in up to 40 clinical centers and will enroll up to 390 patients, and randomizes patients 2:1 to the WorldHeart Novacor LVAS or HeartMate XVE LVAS.
2. DELTA (Destination Evaluation Long-Term Assist) trial will randomize patients in a 2:1 ratio to Micromed Debakey VAD.

Soon, patients will have a variety of devices to choose for destination therapy.

Figure 11.13 (algorithm) outlines the management of patients in end-stage heart failure.

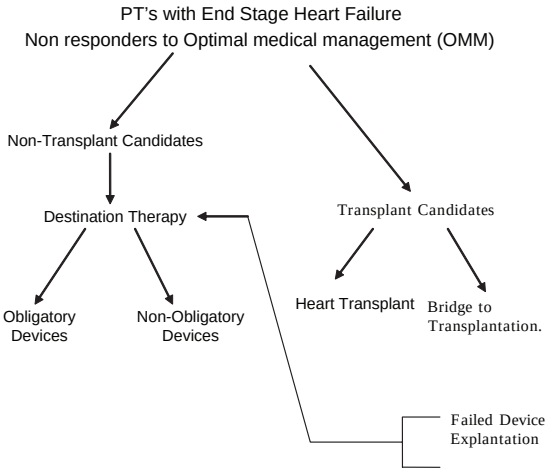


FIGURE 11.13. The management of patients in end-stage heart failure.

Apart from FDA-approved HeartMate for destination therapy), all the other devices discussed in the following section are investigational and available only through clinical trials. Therefore, the proposed algorithm will change as devices proceed along with regulatory approval. The HeartMate XVE is indicated for NYHA class IV patients, who (1) have a BSA > 2.0, (2) are not transplant candidates (historically this has been due to age, renal dysfunction, malignancy, or advanced diabetes), and/or (3) have CHF over at least 60 days

despite optimal medical management. Exclusion criteria include (1) severe biventricular failure or pulmonary hypertension that could lead to right sided failure, (2) aortic/mitral stenosis or aortic valve regurgitation, (3) active infection, (4) severe coagulopathy, and (5) liver dysfunction. In small built patients, the second-generation axial flow pumps might be a good substitute.

Indications for the CardioVAD are broader. The perioperative morbidity and mortality are lower due to a less traumatic nature of the procedure. Manipulation of a diseased heart can totally be avoided in CardioVad placement. It is indicated for a group of patients with less advanced heart failure. Perhaps its role would be in the NYHA class III to IV patients, who have borderline medically refractory heart failure, but enough cardiac reserve to respond to an IABP, with decreased PA pressures and increased cardiac output. Patients failing on inotropes and IABP are not candidates for CardioVAD and would probably benefit from HeartMate or total artificial heart (TAH).

The CardioVAD also requires 14 days for growth of fibroblasts and preparation of the PAD. Although there is no lower limit of the BSA for implantation, there must be at least 9 cm of descending aorta between the left subclavian artery and diaphragm to allow for device placement. The TAH would be preferable in patients who require biventricular support and have significant native cardiac valvular pathology or have terminal acute rejection after heart transplant.

Although there is not enough clinical data to be definitive, these devices can be compared. All the devices reverse heart failure, with the TAH requiring the lowest amount of cardiac medication, followed by the axial flow pumps, pulsatile LVADs, and the CardioVAD. The latter two are assist devices, and the patients will require afterload reduction, diuretics, and beta blockade. Medication can be reduced as peripheral perfusion improves and the heart recovers. Anticoagulation is not required for the CardioVAD or the HeartMate XVE. All other devices require heavy anticoagulation. The risk of thromboembolic event is lowest with the CardioVAD, followed by the HeartMate XVE and highest for the TAH. With regard to mechanical reliability, the HeartMate XVE and TAH require valves which will fail with time. The CardioVAD has the least complicated components that actually get implanted in a patient. The TAH is totally implantable; the axial flow pumps could attain complete implantability once the technology is fully developed. The CardioVAD and displacement pulsatile pumps are not totally implantable, and will have drivelines exiting the patient. Responsiveness to activity, that is, a control algorithm that can increase and decrease the flow as required by the patient, is best developed for the pulsatile LVADs and the CardioVAD (it is triggered by the patients heart rate). Control algorithms for the others devices are being developed. The present model operates in a fixed mode.

The counterpulsation devices are nonobligatory. These can be stopped and started at the patients' discretion. Initially, these devices are operated continuously, as the patients recovers, they can spend prolonged periods off the device. The patients can adjust the need for pumping depending on their symptoms. All other devices are obligatory. The counterpusation devices have the backup of native heart, in case of device failure. The active pump LVADs also have a backup. In the axial flow pumps, VAD regurgitation might prevent the native heart from sustaining enough forward flow. Once stopped, these LVADs cannot be started without a risk of thromboembolic events. The TAH has no backup, and a device failure will be catastrophic. Since the native heart is removed when implanting a TAH, pathology involving the heart does not play a role in device utilization.

The counterpulsation devices are dependent on native heart function, LVADs need adequate right heart function, as well as intact LV valves. Right-sided circulatory failure is a major concern of the active pump LVADs and of minimal concern with TAH. Right-sided heat failure (RSHF) has not been a problem with counterpulsation devices in our clinical experience to date.

Despite tremendous effort and expenditure, the ideal mechanical permanent assist device remains elusive. The three main categories of devices—active pump VADs, counterpulsation, and TAH—have advantages and limitations. The KCV is designed for intervention in advanced NYHA class III patients before there is severe biventricular failure or lack of any myocardial reserve. The KCV can be considered equivalent to a mechanical, permanent, non–energy depleting inotrope and may have a role in stabilizing or improving native

BiopBooks

heart function. However, it is not a device of choice for acute recovery, or, if IABP pumping does not improve hemodynamics. In these scenarios, active pump VADs and TAH excel. As the devices improve and clinical experience with these devices increases, physicians will have the tools to improve the length and quality of life in any patient with end-stage heart failure.

11.5. Key Points to Remember

1. Destination therapy may be considered in elderly patients who are not transplant eligible.
2. Other contraindications to transplantation would also steer patients in this direction.
3. Destination therapy is expensive and limited by complications.
4. Most devices do not last for more than 18 months.
5. Destination therapy is approved by the FDA with the HeartMate device, which is an obligatory LVAD. Other devices awaiting approval include the Novacor LVAD, Abiomed Total Artificial Heart, Kantrowitz CardioVAD, etc.
6. Newer axial flow pumps may have an impact in this space, depending on ongoing trials.

References

1. Hall CW, Liotta D, Henly WS, et al. Development of artificial intrathoracic circulatory pumps. *Am J Surg*. 1964;108:685-692.
2. The RALES Investigators. Effectiveness of spiranolactone added to an angiotensin-converting enzyme inhibitor and a loop diuretic for severe chronic congestive heart failure. *Am J Cardiol*. 1996;78:902-907.
3. The SOLVD Investigators. Effect of enalapril on survival in patients with reduced left ventricular ejection fractions and congestive heart failure. *New Engl J Med*. 1991;325:293-302.
4. The Captopril-Digoxin Multicenter Research Group. Comparative effects of therapy with mild to moderate heart failure. *JAMA*. 1988;259:539-544.
5. Packer M, Bristow MR, Cohn JN, et al. The effect of carvediolol on morbidity and mortality in patients with chronic heart failure. *New Engl J Med*. 1996;334:1349-1355.
6. Frazier OH. Long-Term mechanical circulatory support. In: Edmunds LH Jr, ed. *Cardiac Surgery in Adult*. New York, NY: McGraw-Hill Companies; 1995:1488.
7. Stevenson LW, Rose EA. Left ventricular assist devices: Bridges to transplantation, recovery, and destination for whom? *Circulation*. 2003;108:3059-3063.
8. Dembitsky WP, Tector AJ, Park S, et al. Left ventricular assist device performance with long-term circulatory support: Lessons from the REMATCH trial. *Ann Thorac Surg*. 2004;78(6):discussion 2129-2130.
9. Long JW, Kfoury AG, Sluaghter MS, et al. Long-term destination therapy with the Heartmate XVE left ventricular assist device: Improved outcomes since the REMATCH study. *Cong Heart Fail*. 2005;11(3):133-138.
10. Dowling RD, Park SJ, Pagani FD, et al. HeartMate® VE LVAS design enhancements and its impact on device reliability. *Eur J Cardiothorac Surg*. 2004;25(6):958-963.
11. Stevenson LW, Kormos RL, Bourge RC, et al. Mechanical cardiac support 2000: Current applications and future trial design: June 15-16, Bethesda, Maryland. *J Am Coll Cardiol*. 2001;37:340-370.
12. Chen JM, Levin HR, Rose EA, et al. Experience with right ventricular assist devices for perioperative right-sided circulatory failure. *Ann Thorac Surg*. 1996;61(1):305–310; discussion 311-313.
13. Rao V, Oz MC, Edwards NM, Naka Y. A new off-pump technique for thoratec right ventricular assist device insertion. *Ann Thorac Surg*. 2001;71(5): 1719-1720.
14. McCarthy PM. HeartMate implantable left ventricular assist device: Bridge to transplantation and future applications. *Ann Thorac Surg*. 1995;59: S146-S151.
15. Van Meeter CH. Right heart failure—Best treated by avoidance. *Ann Thorac Surg*. 2001;71:220-222.
16. Kantrowitz A. Challenge to conventional treatment for myocardial failure-mechanical assist. *Biomater Med Devices Artif Organs*. 1976;4(1):1-20.
17. Antonatos PG, Anthopoulos LP, Vrettos AN, Moulopoulos SD. The use of a small intra-aortic balloon to increase coronary flow. *Life Support Syst*. 1983;1(3):151-164.
18. Nanas JN, Nanas SN, Kontoyannis DA, et al. Myocardial salvage by the use of reperfusion and intraaortic balloon pump: Experimental study. *Ann Thorac Surg*. 1996;61(2):629-634.

12
Enabling Techniques and Technologies

Patricia Gramling-Babb, Valluvan Jeevanandam, Jai Raman, David Song, Hilton M. Hudson II, and John Paul Williams

This chapter focuses on operative techniques and perioperative methods that facilitate high-risk surgery for heart failure in special circumstances. They include operative techniques such as

1. Beating Heart Surgery in the setting of heart failure.
2. Proactive management of impending right heart failure, including Inhaled Nitric Oxide and/or Right ventricular assist devices.
3. Prophylactic Sternal Plating to reduce the risk of mediastinitis.
4. Sternal sparing incisions—mini-thoracotomy incisions for mitral and tricuspid valve procedures.
5. Complex Tricuspid Valve Repair for Pacer-defibrillator related tricuspid regurgitation (TR).
6. Prophylactic DeVega Tricuspid Valve Annuloplasty in Heart Transplant recipients.
7. High Thoracic Epidurals to facilitate quick recovery in patients with impaired lung function.

12.1. Beating Heart Surgery

The primary causes of myocardial dysfunction in the high-risk patient with heart failure may be global ischemia caused by aortic cross-clamping, and activation of the systemic inflammatory syndrome by cardiopulmonary bypass. If the patient requires surgical revascularization, off-pump coronary artery bypass (OPCAB) surgery delivers on all counts by avoiding the "pump" and the aortic cross-clamp. OPCAB is actually dealt with in detail in a separate chapter. Many of the patients who need surgery for heart failure often require combined surgery, which may include varying combinations of CABG, left ventricular reconstruction, mitral valve surgery, tricuspid valve surgery, etc.

While in the majority, cardioplegic arrest of the heart preserves myocardial function such that myocardial recovery is assured at the end of the procedure, certain specific situations may be associated with marginal cardiac recovery. This is especially true in the postinfarct setting or in the setting of acute heart failure decompensation with a background of poor ventricular function.

Our own experience in this group of patients numbers over 100 in the past 4 years. All of these patients had poor ventricular function in the setting of an acute exacerbation of heart failure. A quarter of them were in cardiogenic shock and 20% had established renal dysfunction.

All of them had beating heart cardiac surgery that included CABG, left ventricular reconstruction, mitral valve repair, tricuspid valve repair, etc., in various combinations. About 30% of these patients had off-pump CABG, while the others had a combination of procedures on pump with the heart beating. While suturing on a heart that is beating is technically challenging, these procedures can be done providing the surgeon takes care in handling the tissues. For instance, tying down a mitral valve prosthesis or ring can be particularly difficult in elderly female patients with fragile tissues. In our series, there were four deaths when the expected mortality was close to 25%.

This can be a technically demanding feat, especially in fragile old patients or in the setting of redo surgery. However, in capable hands, this technique helps preserve the myocardium and has a low chance of requiring additional mechanical support

DropBooks

of the heart at the conclusion of the procedure. A rising lactate level on cardiopulmonary bypass is a very poor prognostic sign and one that is associated with a mortality of over 90% in our experience. The only instances when patients have survived in this instance have been when the lactic acidosis is induced by an occult lymphoid malignancy such as non-Hodgkin's lymphoma.

12.2. Proactive Management of Right Heart Failure

12.2.1. Right Heart Failure is a Condition Best Treated by Avoidance

This is an important adage, especially relevant to surgery for heart failure. The following paragraphs outline measures that can be used to minimize right heart dysfunction or treat it before it progresses to an irreversible, fatal outcome.

Assessment of right ventricular function is a composite of visual inspection of right ventricular contraction directly and by echocardiography. Additional guides are the pulmonary artery pressures and right atrial pressures.

Careful management of right heart function includes the following:

– Avoidance of overfilling and overdistension of the right ventricle, by large fluid boluses. In cases where there is a persistently high central venous pressure (CVP), aquapharesis or hemofiltration may serve a quick and easy way of getting fluid off and improving right heart function.
– Careful attention to myocardial protection in patients undergoing procedures with cardioplegic arrest. Frequent doses of blood cardioplegia at 10–15-min intervals certainly help. Antegrade blood cardioplegia preserves right ventricular function better than do retrograde cardioplegia. In cases of right coronary artery disease, infusing cardioplegia down the grafts to the right-sided coronary arteries regularly help with protection. Minimizing cross-clamp time aids in right ventricular recovery. Adequate de-airing of the heart avoids "air-hits" to the right coronary circulation, further preventing deterioration when preparations are being made to separate from cardiopulmonary bypass.

Preemptive tactics:

– When the patient has high pulmonary artery pressures preoperatively, we prophylactically use Milrinone loaded on pump, or inhaled nitric oxide while the patient is being weaned off CPB.
– Optimizing atrioventricular synchrony by using biatrial and biventricular pacing to ensure a controlled rate and rhythm. If the patient is in atrial fibrillation or an uncontrolled rhythm going into the procedure, amiodarone is infused during the pump run to ensure proper loading of the patient.
– Intra-aortic balloon counterpulsation is often used to optimize right ventricular function in the setting of preexisting right ventricular dysfunction.
– Correction of TR to ensure that the patient is weaned off with only trivial to mild degrees of TR.
– At early signs of right ventricular dysfunction, we consider inhaled nitric oxide. If that fails, a decision is made to use mechanical right ventricular assistance.

12.3. Prophylactic Sternal Plating: Sternal Closure with Titanium Plate Fixation—A Paradigm Shift in Preventing Mediastinitis

Sternal instability predisposes to postoperative mediastinitis. Biomechanical studies have shown the superiority of rigid plate fixation over wire-circlage in sternal healing. We studied rigid plate fixation for sternotomies in high-risk patients.

High-risk patients were identified as those having three or more historically established risk factors for postoperative mediastinitis, such as chronic obstructive pulmonary disease (COPD), reoperative surgery, renal failure, diabetes, steroid use, obesity, existing infection, and immunosuppression. Three hundred twenty high-risk patients had prophylactic rigid plate fixation (groups S) between July 2000 and January 2005. The Control group (groups C) comprised 215 patients with similar risk profiles who were not plated during 2000 and 2001.

Average age, male–female ratio, risk factors, and type of procedures were similar in both

groups. Follow-up ranged from 4 to 200 weeks. There were 12 perioperative deaths (3.75%) in group S and 8.6% (18 patients) in group C. There were no instances of deep mediastinitis in group S. Group C had mediastinitis in 28 (13%, $p < 0.05$), requiring high-dose antibiotics and plastic surgical intervention.

Sternal fixation with titanium plates is an effective way of ensuring sternal immobility, thereby reducing the substrate for bony infections. Application of this technique in high-risk patients prevents mediastinitis.

12.3.1. Introduction

Sternotomies are the most frequently performed osteotomies worldwide. Traditionally, cardiothoracic surgeons have been trained to close or approximate the sternum with wire-circlage. Despite improvements in the understanding of principles of rigid fixation with plates, these changes have not been applied to sternal closure, widely. Based on biomechanical studies in a bone analog model, plates and screws were adapted for use in sternal closure. Infectious complications leading to post-sternotomy mediastinitis are extremely morbid and the mortality rate can be as high as 15%.[1] Methods for preventing post-sternotomy mediastinitis have included prophylactic measures including antibiotic therapy and various means of skin closure. Few have focused on rigid osseous fixation as a means for preventing infection despite experimental evidence to support it.[2]

Since Julian reintroduced Milton's (1897) operation of median sternotomy in 1957,[3] numerous methods for sternal osteosynthesis have been described. Despite evidence of the superiority of rigid plate osteosynthesis, the current standard for sternal closure remains circlage wire fixation. Because of the proven merits of increased stability and decreased incidence of nonunion, malunion, and infection, the principles of rigid fixation have caused paradigm shifts away from wire fixation of bone, in other areas. Circlage fixation under normal physiologic loads can prove to be inadequate, leading to separation.[4] Bacterial contamination in the face of sternal instability can then progress to deep sternal wound infections and mediastinitis. Effective rigid osteosynthesis of the sternum may prevent post-sternotomy mediastinitis from occurring by affording stability, promoting primary healing of the sternum.

We adopted this technique of rigid plate fixation by modifying plates that were used in mandibular fixation.

We had earlier reported on our preliminary experience with the use of titanium plate fixation of the sternum.[5] We now report on our evolving experience in this area.

12.3.2. Patients and Methods

A system of plates and screws was developed for specific use in the sternum by the W Lorenz Corp (Jacksonville, Florida), called the Sternalock system. The screws that were initially developed required predrilling of the bone and were bicortical. These were eventually changed to monocortical, self-tapping screws.

Between July 2000 and January 2005, 320 patients underwent internal fixation of the sternum with the Sternalock system. This system of plating was applied in patients who were considered high-risk based on previously described risk criteria for deep sternal wound infection.

Preoperative risk factors included

- Diabetes mellitus,
- COPD,
- Obesity (BMI > 30),
- Renal failure,
- Chronic steroid use,
- Concurrent infection and acquired or iatrogenic immunosuppression,
- Immunosuppression, and
- Redo sternotomy.

Intraoperative risk factors included

- Off midline sternotomies,
- Osteoporosis,
- Long cardiopulmonary bypass runs (of greater than 2 h), and
- Transverse fractures of the sternum.

If three or more of these factors were present, the patient's sternum was internally fixed with plates and screws that were part of the Sternalock system.

Cardiac surgeons selected all patients and rigid plate fixation was applied immediately after the cardiac procedure.

DropBooks

12.3.2.1. Surgical Technique

Care is taken to ensure a midline sternotomy. The presternal pectoral muscles are mobilized of the sternum over the body of the sternum. One figure-of-eight wire is placed in the manubrium and one in the region of the xiphisternum. The sternal halves are carefully aligned and approximated with a combination of the wires and bone reducing forceps placed in the second and fifth intercostal spaces. The plates are then seated in such a way that they straddle the sternal halves. The plates are then secured into the bone with the appropriate self-tapping screws.

As the procedure and comfort level with plating evolved, plates were secured to the body of the sternum, while figure-of-eight wires were placed in the manubrium and xiphisternum. Figure 12.1 is an artist's rendition of a plated sternum.

Patients were followed up clinically and their sternal wounds assessed both during their hospital stay and in the outpatient follow-up setting. Patients were followed by the cardiac surgical team and managed irrespective of the sternal closure. Criteria for discharge and routine follow-up care did not vary. Successful sternal closure was defined by physical examination devoid of instability, pain, wound healing complications, and radiographs showing unchanged location of hardware for a minimum of 8 weeks.

For purposes of comparison, patients who underwent plate fixation were classified in group S and compared to a similar group of patients ($n = 215$) who underwent standard wire closure in 2000 and 2001, selected on the basis of their risk profiles Figure 12.1 is a schematic of the sternal plates on the sternum and Figure 12.2 is an operative photograph of a plated sternum. These patients were classified as group C.

A biostatistician performed the statistical analysis using statistical analysis software (SAS) software. Fischer's exact test was used to assess statistical significance and a 'p' value of < 0.05 was considered significant.

12.3.3. Results

Patients were followed up between 4 and 200 weeks. Patients referred to us from other centers were discharged with a specific note about the sternal plates and the need for us to be contacted if there was a problem with the plates (specifically if the plates needed to be removed or the sternum reopened).

Demographic characteristics, risk factors, and operative procedures were similar in the two groups.

During the same study period, analysis of a similar cohort of high-risk patients (group C) showed that had mediastinitis, as defined by the presence of positive deep sternal wound cultures and systemic sepsis (13% of 205 patients, $p < 0.05$). This required high-dose antibiotics and plastic surgical interven-

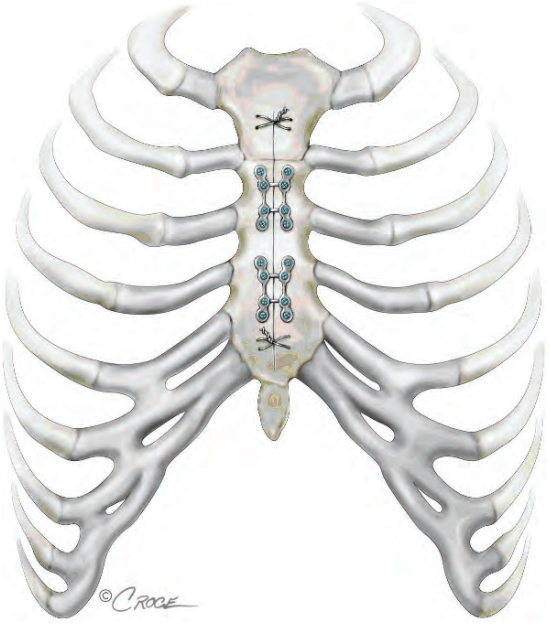


FIGURE 12.1. Sternum closed with a combination of wires and plates.

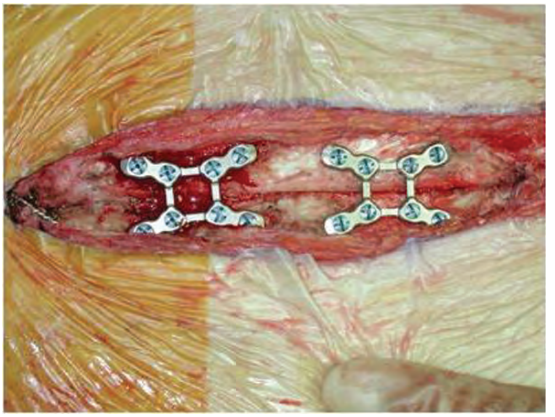


FIGURE 12.2. Operative photograph of plated sternum.

tion. Mortality of 8.6% (18 patients) was noticed in group C. The age, gender, and risk factor distribution were very similar to those in the study group. All of these patients required surgical debridement, sternectomies, and pectoral muscle flap closure. Of the 18 deaths in group C, 2 were attributed to post-sternotomy mediastinitis. The total number of adult cardiac procedures during the control study period was 671 and the total incidence of post-sternotomy mediastinitis was 4.2%.

There was no mediastinitis in the study group (Fisher's exact test $p = 0.0002$).

There were five instances of sterile sternal dehiscence (1.5%) in the presence of sternal plates. None of these patients had evidence of infection by wound culture. The first patient had very strong bone and the plating system was an early version with small screws that ripped out of the sternum. The second patient was also a very muscular patient in whom the screws seemed to rip out. Both these patients had intractable postoperative coughing. The other three patients were elderly diabetics with significant osteoporosis. The screws were not able to find proper purchase in their very soft bone. Alternative strategies are being developed for this select but high-risk population.

The log rank test was not used because of the relatively small number of patients in the study group and the disparate nature of the groups.

DropBooks

12.3.4. Discussion

Few proven measures have been developed for the prevention of mediastinitis. This is despite many strides that have been made in the management of post-sternotomy mediastinitis. Existing modalities focus on adjunct methods to prevent bacterial contamination from both the surgical team and the patient.[6] Focusing on a more stable and successful technique of sternal osteosynthesis in an effort to prevent complications has been cited. Most revolve around a different pattern of wire-circlage or various nonrigid methods of closure.[7] Rigid plate fixation of the sternum, although not new, has not been widely used as the optimal method of sternal osteosynthesis for various reasons.

Some of these include added time and expense, the difficulty of emergent reentry, and the availability of a simple and effective plating system. One obstacle for the acceptance of rigid plate fixation to the sternum has been the logistics of drilling into the sternum. This has been circumvented by developing a system of self-tapping screws. The screws are selected on the basis of sternal thickness and we have switched to monocortical screws. This means securing the anterior table of the sternum after lining it up appropriately.

A second obstacle has been the issue of emergent reentry into the mediastinum for hemorrhage. The SternaLock plates are specifically designed to be cut in the middle with standard wire cutters found in any reentry tray. Salvage of the closure can then be performed with new plates and without redrilling by exchanging the 2.4-mm screws for 2.7-mm emergency screws. These plates are made of titanium and do not interfere with magnetic resonance imaging. They are clearly radio-opaque and readily visible on X-ray imaging.

A third obstacle to wide acceptance has been the cost of hardware placement and the additional time it takes to implant hardware. While the implants are more expensive than wires, the time taken to implant them is now less than wiring. At our institution, the average additional hospital charge for patients suffering from post-sternotomy mediastinitis is just over $500,000. Prevention of post-sternotomy complications not only can be fiscally sound, more importantly, it can potentially decrease the morbidity and mortality associated with this complication. The cost of the plates ranges from $700 to about $900 depending on the number of plates and screws used.

Efficient plating systems for many other bones abound; a plating system specifically designed for the sternum was first described by us in 2003. Previous attempts at rigid plate fixation of the sternum had employed mandibular reconstruction plates or fracture mini-plates with some success, but issues of emergent reentry and accurate precision placement were not addressed.[8] Furthermore, fashioning mandibular reconstruction plates for the sternum was cumbersome as each plate had to be cut specifically for each region of the sternum.

The benefits of rigid plate osteosynthesis have caused paradigm shifts away from wire fixation for orthopedic and plastic surgeons over 20 years ago. More recently, neurosurgeons have adopted plate fixation of bone flaps in the past 5 years. Cardiac surgeons are the only surgeons who continue to

fix bone with wire-circlage. Ironically, cardiac surgeons perform the sternotomy, which is the most common osteotomy worldwide. Yet, as a group we have not adopted the state-of-the-art techniques in stabilizing this osteotomy. In the setting of a surgically created osteotomy or fracture treatment, a failure rate even less than 5% might be considered unacceptable but may be tolerated by the patients. However, in the setting of the sternotomy, this failure rate may have devastating complications such as nonunion, persistent pain, and deep sternal wound infection.

Complications of median sternotomy have been reported ever since the early and widespread adoption of this common technique.[9] Sternal stability has always been regarded as essential for normal healing of these wounds. There was a report from our unit in 1994 on the use of rigid internal fixation in postoperative mediastinitis, with bony union being achieved in more than 90% of patients.[9] Others have used plates to provide a template for more rigid fixation[10] in sternal dehiscence. Cyanoacrylate glue has been used in mediastinitis even with the risk of toxicity in an attempt at improving sternal stability.[11] Negri and coworkers evaluated a new technique using thermoreactive clips that seemed to improve the rate of wound infection but did not eliminate it.[12] Our approach was to use the best existing techniques of osteotomy closure and adapting them to the sternal situation. As we grew more familiar with the technique of rigid plate fixation, we made modifications. We found that using a figure-of-eight wire in the manubrium and the xiphisternum assisted in approximation of the bone along with the reducing forceps. We found this combination approach to be cost-effective and efficient. Therefore, many of the patients received two wires and two plates.

On the basis of our early success in a high-risk population with a historically high rate of complications, we embraced the concept of rigid plate fixation. This report highlights the fact that rigid plate fixation can dramatically reduce sternal wound infection if used prophylactically in high-risk patients. While it may not eliminate sternal deshiscence completely, it can provide a way to ensure secure closure in a variety of patients who are at increased risk of wound infections and poor healing.

12.4. Key Points to Remember

Sternal fixation with custom-made plates is a safe and effective technique. Experience with this technique of rigid sternal osteosynthesis has shown a dramatic reduction in wound infections associated with sternotomies in high-risk patients. Consider rigid plate fixation of the sternum in patients with obesity, diabetes, COPD, immunosuppression, redo surgery, and multiple sternal fractures.

12.5. Sternal Sparing Incisions—For Aortic, Mitral, and Tricuspid Procedures (Mini-Thoracotomy Approach)

This approach is a by-product of the “robotic” push. In the lead up to our own robotic program, we went through a learning phase and eased into it by performing a range of “mini-mitral” procedures.

The absolute indication for this approach seems to be the complex redo mitral or tricuspid procedure in a patient with patent coronary artery grafts. The use of these techniques avoids unnecessary dissection around the ventricles, damage to patent grafts and other cardiac structures. It is very possible to hone in on the valve concerned, either mitral or tricuspid. Since the morbidity of these procedures is remarkably less than those of redo sternotomies, patients tolerate these much better. In our experience, there is a trend toward lower mortality with a dramatic reduction in morbidity.

Details of this procedure include the following:

- Double lumen endotracheal tube.
- Appropriate positioning with the patient’s right side up at 45° and the right arm positioned abducted and supported along a crossbar (Figure 12.3).
- The right groin is marked after the patient is positioned, so that the femoral artery and vein can be easily dissected out for cannulation through a small oblique incision.
- The chest is marked to outline the right border of the sternum, the second, third, and fourth intercostal spaces (Figure 12.4).
- The right lung is deflated and the chest entered, usually through the fourth intercostal space for



FIGURE 12.3. Positioning with skin marked and arm being positioned.



FIGURE 12.4. Skin markings to get orientation in the right chest.

the mitral and the second or third intercostal space for the aortic valve. Simultaneously, the right groin is opened through a small oblique incision to prepare the femoral vessels for cannulation.

- The pericardium is opened, and hitched up to the chest wall. The right atrium and superior vena cava are then identified. The interatrial groove is then developed.
- The right femoral vein and artery are cannulated in sequence under transesophageal echocardiographic guidance. The venous line has a "Y" attachment to allow an additional cannula to be placed in the superior vena cava through the thoracotomy incision.
- The patient is then connected to cardiopulmonary bypass through the cannulae in the groin with additional direct drainage through the SVC.
- Further dissection of the atrium and aorta is carried out. Attempts are made to dissect out the aorta to allow a transthoracic clamp to be applied midway along the ascending aorta.
- A cardioplegia is placed low on the ascending aorta and the aorta then clamped.
- The atrium is then opened and the appropriate valve procedure performed (Figure 12.5).
- A 5-mm thoracoscope is inserted from below the incision through a separate port and the screen placed directly in front of the primary surgeon.
- The ventricular pacing wires are placed before the patient is weaned off cardiopulmonary bypass.
- If the aortic cross-clamp cannot be applied, the patient is cooled to 28 °C and the procedure performed with the heart beating.
- De-airing is aided by using carbon dioxide insufflation at about 1–2 L/min.
- Prior to removal of the cross-clamp, the left lung is inflated and air evacuated.
- Once the procedure is completed, and the patient weaned off CPB, the scope is used to visualize all the areas inside the chest wall where instruments have passed through to ensure no bleeding points are missed.

DropBooks

12.6. Key Points to Remember

Mini-thoracotomy is a very useful approach in complex redo patients.

This approach can dramatically reduce the morbidity in most patients undergoing aortic, mitral, and/or tricuspid valve procedures.

12.7. Complex Tricuspid Valve Repair in Patients with Pacer-Defibrillator Related Tricuspid Regurgitation

12.7.1. Introduction

The tricuspid valve is almost always traversed when a permanent pacemaker is implanted through the transvenous route. Despite the knowledge that mild degrees of TR can be caused by the

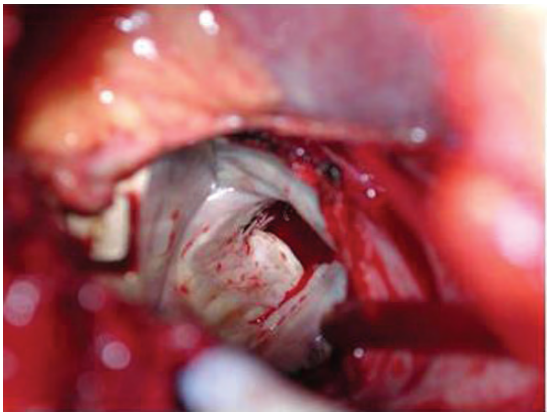


FIGURE 12.5. View of the mitral valve through a mini-thoracotomy.

ventricular lead going across the right-sided atrioventricular valve,[13] this often does not have a clinical consequence. Occasionally, pacing leads were known to have caused severe TR.[14] Better lead design in the 1980s corrected this potential problem, making ventricular leads unlikely to cause TR in most patients.

The lifesaving properties of implantable cardioverter-defibrillators in patients with poor ventricular function have been effective in reducing the risk of sudden cardiac death.[15] Despite the evidence of these expensive devices being effective predominantly in patients with ischemic heart disease who have suffered a significant myocardial infarction, there is widespread use in many patients with poor ventricular function. Be that as it may, these implantable cardioverter-defibrillators seem to confer a survival benefit.[16] Patients who have poor ventricular function and heart failure are now increasingly being referred for surgical intervention. Some of them present with TR of varying grades in addition to their underlying myocardial and valvular conditions. When patients with these devices implanted in them present for surgery, they present a conundrum. Do we operate on these tricuspid valves, which if we leave alone can cause significant morbidity and/or mortality? Repair of these tricuspid valves can be difficult because the valvular regurgitation is frequently caused by the stiff ventricular cardioverter-defibrillator lead impinging on the septal leaflet and not due to annular enlargement.[17]

The other option, namely, tricuspid valve replacement, is an option with major problems not the least of which is that the cardioverter-defibrillator needs to be changed to a suboptimal epicardial system. Controversy exists about the kind of valve to use, even though both bioprosthetic and mechanical valves are uniformly poor in long-term outcomes.[18]

We describe a new technique that preserves the leads, the tricuspid valve leaflets, and mechanism with an annuloplasty to deal with this condition. This publication details our early experience with this technique.

12.7.2. Patients and Methods

Our experience started in January 2005 and we studied patients up to July 2006. During this period, at the University of Chicago, 27 patients underwent complex tricuspid valve repair for TR in the presence of previously implanted transvenous cardioverter-defibrillator leads. All of the patients were symptomatic with NYHA class III or IV: The mean age of the patients was 67 years, ranging from 38 to 80 years. Fifteen of these patients or 55% underwent redo surgery. Seven of these patients underwent procedures through a right mini-thoracotomy. Five of them had the redo procedure for the third or fourth time. Associated procedures included mitral valve reconstruction in 21 patients, CABG in 11 patients, left ventricular reconstruction in 8 patients, and aortic valve replacement in 3 patients.

12.7.2.1. Surgical Technique

The right atrium was opened with a longitudinal incision and the tricuspid valve assessed. Stay sutures were placed above the valve annulus in the atrium to display the valve. The mechanism of TR was assessed with the heart beating on cardiopulmonary bypass once it was established that the TR was predominantly due to the cardio-defibrillator lead pushing the septal leaflet into the right ventricular carity and preventing it from coapting with the other leaflets. Figure 12.1 is an intraoperative photograph demonstrating the stiff defibrillator lead pushing on the septal leaflet as it traverses the tricuspid annulus (Figure 12.6).

The pacer-defibrillator lead is then mobilized and freed of any adhesion to the leaflets. The lead is then positioned in the potential “cleft” between the septal and inferior leaflets of the tricuspid valve. This “cleft” is then closed over the lead with one or two 5/0 Ticron sutures. The tricuspid annulus is then repaired with a ring or suture annuloplasty. If the annulus is significantly dilated, a flexible St Jude Tailor

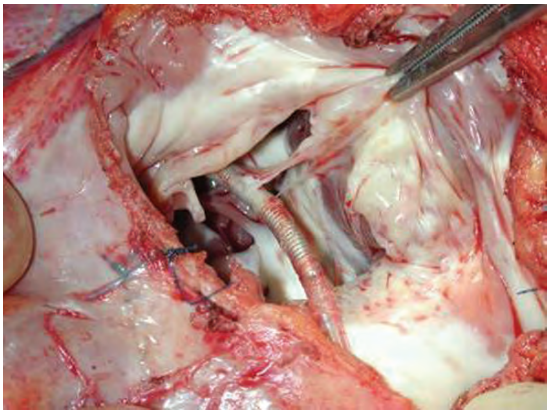


FIGURE 12.6. Operative photograph of pacer-defibrillator lead traversing tricuspid valve.

ring is implanted with multiple 2/0 Ticron sutures placed through the annulus, just encroaching on to the edges of the annulus subtended by the septal leaflet.

Figure 12.2 shows the steps of this operative technique. If the annulus is not grossly enlarged, the annulus is bolstered with a pledgetted 3/0 polypropylene suture to get a measured annuloplasty to about 28–29 mm (Figure 12.7).

Steps of the repair are as follows:

1. Mobilized defibrillator lead and the leaflets of the tricuspid valve.
2. The lead repositioned in the cleft between septal and inferior leaflets with a suture approximation of the leaflets above the cleft.
3. The repositioned lead with cleft closure and a tricuspid valve annuloplasty.

In our series presented here, 7 patients had a DeVega-type suture annuloplasty while the other 20 had a flexible ring annuloplasty.

Limitations: This technique requires normal and pliable leaflets. If there is fibrosis of any of the leaflets or if there is significant subvalvar fibrosis, this technique may not be applicable. This procedure is best performed when the right ventricular function, even if impaired, is recoverable. Large, poorly contractile right ventricles might be very poor substrates for any kind of tricuspid intervention.

12.7.3. Results: There were no Deaths

There were perioperative deaths. Mean TR preoperatively was 3.8 and fell to a mean of 1.2 immediately after the surgery. Similarly, the mean CVP fell from

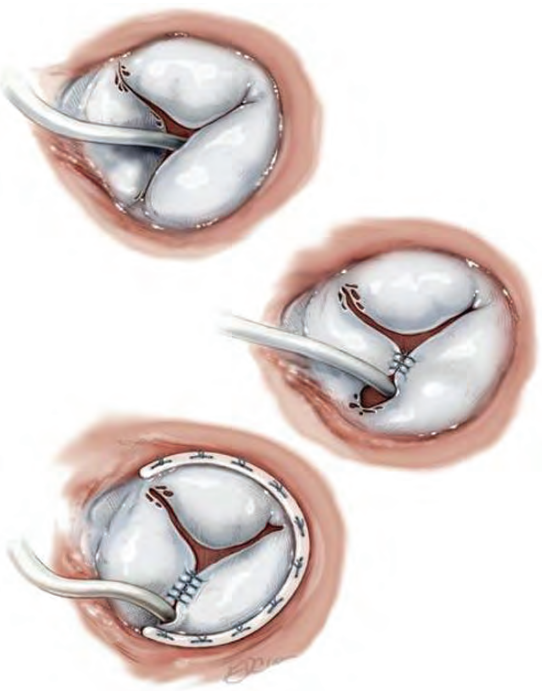


FIGURE 12.7. Steps of tricuspid repair.

34 mmHg preoperatively to 12 mmHg, postprocedure. All patients had resolution of symptoms and signs of right-sided failure. Perioperatively, the elevated CVP did cause either an overt or a subclinical picture of liver dysfunction. Eight patients had impaired liver function tests with severely enlarged livers and pulsatile hepatomegaly. This liver dysfunction caused a significant perioperative coagulopathy.

Patients were followed up with postoperative echocardiograms. The mean postoperative stay was 11.5 days (ranging from 5 to 43 days). Three patients required tracheostomy and prolonged ventilation. At a mean follow up of 24 weeks (range 4–80 weeks), the mean degree of TR was 1.5.

Since this is a new technique with the period of follow-up being short, we have not attempted to compare the outcomes with standard tricuspid valve surgery. However, the lack of early mortality in this complex group of patients was very encouraging. The morbidity was in keeping with a very complex and sick group of patients.

12.7.4. Discussion

Tricuspid valve regurgitation has a known association with right ventricular pacing[19] but over

DropBooks

the years, improvements in design have reduced this risk. Pacemaker leads have improved in design and flexibility, and do not overtly cause TR. As a consequence, pacemakers are put in quite liberally without much thought given to possible valvular consequences. More recently, the cost and survival benefit of pacer–cardioverter-defibrillators in preventing sudden death[20] has led to increased use of these devices. Even though the benefit of these devices was shown in patients who were postmyocardial infarction, there is a general trend to implant these devices in all patients with low ejection fractions. The problem posed by the increased use of these pacer-defibrillators and their impact on TR was highlighted in a recent publication from the Mayo Clinic.[21] As this publication mentions, not all cases of TR with pacer-defibrillators have the same mechanism causing the leakage. However, the majority of patients in this series had evidence of the stiff lead pushing down on the septal leaflet keeping it stented in an open position, thereby preventing coaptation with the other two leaflets during closure. We saw this initially in a patient on whom we performed a ring annuloplasty of the tricuspid valve with a very good perioperative result. However, over a period of a few weeks, the TR returned. A series of follow-up echocardiographic studies actually showed the lack of septal leaflet coaptation due to the pacer-defibrillator lead pushing on it. A similar finding was noted in a group of our heart failure patients with exacerbation of right-sided failure following insertion of pacer-defibrillator leads. When we dealt with a few of these patients presenting for surgery on other valves or coronary arteries, this posed a clinical conundrum. To secure a good operative and durable long-term result, it is important to deal with the TR. One option would be to replace the tricuspid valve and take out the transvenous cardioverter-defibrillator and change it to an epicardial system. This has two major flaws, namely:

– Poor short- and long-term outcomes with tricuspid valve replacement.[22]
– Epicardial pacer-defibrillator systems that are not commonly used and may be complicated.[23]

The septal leaflet plays an important role in the competence of the tricuspid valve,[24] from a developmental and practical point of view. Tethering of tricuspid valve leaflets can account for residual regurgitation after repair.[25] There are other factors that also may account for residual TR,[26] which are hopefully addressed at the time of surgery. Intraoperatively, while dealing with the tricuspid valve, the two issues that we can address easily are the lead impingement on the septal leaflet both in the acute and chronic setting and the annular dimensions. Therefore, we came up with this technique whereby the lead is repositioned in the potential cleft between septal and inferior leaflets. The lead is then retained in that position by a fine edge-to-edge suture that closes the cleft over the lead. These edge-to-edge leaflet approximations seem to work well in the tricuspid valve, as long as the leaflets are normal and the approximating suture utilizes small segments of valve leaflets.[27] The annulus was stabilized with a ring annuloplasty if there was significant annular enlargement above 35 mm. If the annulus was marginally enlarged, we elected to use a DeVega-type suture annuloplasty.

While our results with this technique have been encouraging, it is important to select patients carefully. Our recommendations are to consider this kind of repair in patients with severe TR in the presence of transvenous pacing-defibrillator leads, preserved leaflets, and reasonable right ventricular function. This repair would not work if the leaflets or the subvalvular chords were abnormal. We would also recommend avoiding this repair in patients with poor right ventricular function.

12.8. Key Points to Remember

Tricuspid regurgitation in patients with heart failure and the presence of pacer-defibrillator leads is most commonly due to the lead impinging on the septal leaflet and progressive annular dilatation. Our method of repair is to mobilize the lead, reposition it in the cleft between the septal and inferior leaflets of the tricuspid valve. The lead is then secured in position with a suture closing the "cleft" over the lead with sutures and correcting the annular enlargement with a flexible ring or suture. Results so far remain encouraging.

12.9. Prophylactic DeVega Tricuspid Valve Annuloplasty in Heart Transplant Recipients

12.9.1. Introduction

Orthotopic heart transplantation (OHT) is often associated with the development of tricuspid regurgitation (TR),[28,29] with the reported incidence varying from 47 to 98%.[30–32] The TR can be related to structural or functional factors. The standard biatrial technique of OHT (sOHT) is associated with more TR than the bicaval (bOHT) technique. This difference is attributed to alteration in the geometry of the tricuspid valve and right atrium related to the technique of right atrial anastomosis. Other possible causes of TR include (1) allograft dysfunction with right ventricular dilatation due to poor preservation, reperfusion injury, donor factors, or rejection, (2) pulmonary hypertension, (3) severe donor recipient size mismatch, and (4) structural damage occurring during endomyocardial biopsy.[33,34] Moderate and greater grades of TR are associated with right-sided heart failure symptoms, renal and hepatic dysfunction, and decreased long-term survival.[35,36] It remains unclear whether the TR is a reflection of poor allograft function or a primary abnormality, but once present, repair or replacement is often indicated. Renal dysfunction is also a long-term consequence of OHT. This is most commonly attributed to the calcineurin inhibitors and may also result from TR.[37,38]

The DeVega-type of tricuspid annuloplasty using a suture has been used to treat TR. It is simple, quick, inexpensive, and durable.[39] We have previously reported short-term results on a population of randomized and prospectively studied patients, one group who received prophylactic DeVega tricuspid valve annuloplasty (TVA) to prevent TR after OHT.[40] We demonstrated less TR and improved perioperative heart function and survival. This chapter reports on the long-term (6 year) follow-up of these patients and compares them with regard to survival, amount of TR, renal function, and hemodynamics.

12.9.2. Methods

12.9.2.1. Study Design

Of the 87 patients receiving heart transplants at Temple University Hospital between April 1997 and April 1998, 60 patients met selection criteria for this comparison. Institutional Review Board permission was received (March 1997) before studying these patients. Twenty-seven patients were excluded because of (1) multiple organ transplantation, (2) retransplantation, (3) donor/recipient weight ratio of < 0.5, (4) pulmonary vascular resistance (PVR) of > 4 Woods units, (5) greater than mild TR documented on donor echocardiography, (6) donor ejection fraction of <35%, (7) donor coronary artery disease requiring revascularization, and (8) donors requiring two inotropes or dopamine at > 12 mcg/kg/min. In accordance with our practice at that time, these patients who were deemed higher risk as evidenced by one or more of the listed factors routinely received TVA before the transplant procedure.

Two surgeons performed the procurement and implantation during this time period, and the procedures were evenly distributed among them. TVA was performed during preparation of the donor heart. In order to ensure consistency and standardization, only one of the surgeons performed the TVA. By strictly adhering to an evenly distributed procurement call schedule, randomization was achieved. Patients were not included in the comparison if unforeseen circumstances caused deviation from the on-call schedule. In the majority of cases, implantation was a combined effort of the two surgeons. The patients received an OHT (group STD) or OHT with TVA (group TVA). Data were obtained prospectively and data analysts were blinded to the assignment of patient groups. Data analyzed included operative and donor information, survival, amount of TR, hemodynamics, serum blood urea nitrogen (BUN), and creatinine.

12.9.2.2. Procedure

The University of Wisconsin (Barr Laboratories, Pomona, NY) solution was used for cardioplegia and preservation solution. The recipient cardiectomy and recipient–donor anastomoses were done using the bicaval technique described by Sarsam et al.[41] and others.[19] All patients received a baseline inotropic regiment of T3 (0.08 mcg/kg bolus, infusion 0.08 mcg/kg for 3 h), 5 mcg/kg/min of dobutamine, and 3 mcg/kg/min of dopamine. Any increase above baseline was considered as elevated inotropic requirement. Patients were considered weanable from CPB if they

DropBooks

could sustain a mean systemic blood pressure of >70 mmHg with a CVP of <15 mmHg and a cardiac index (CI) of >2.1 L/min/m^2 with a combination of inotropic and Intra-aortic Balloon Pump (IABP) support.

Group TVA patients received a DeVega-type annuloplasty on the donor graft prior to implantation. The tricuspid valve was visualized through the inferior caval or right atrial opening and a double layer of pledgeted 2-0 polypropylene was used to stabilize the annulus. The annulus was sized to a 29-mm dilator. If the annulus was less than 29 mm, it was stabilized to a size just a little smaller than the native annulus. This procedure is shown in Figure 12.8.

12.9.2.3. Management

All patients received triple-drug immunosuppression therapy with cyclosporine (CyA) (3.5–5.0 mg/kg/day), azathioprine (1.5–2.5 mg/kg/day), and steroids. Induction therapy was not routinely used. Patients either had the CyA switched to tacrolimus or had mycophenolate mofetill substituted for azathioprine for repeated rejection. CyA therapy was adjusted to maintain serum trough levels of 250–300 ng/ml during the first year after hypertension (HT). Azathioprine dose was adjusted to maintain white blood cell counts of > 4,000 ml^{-1}. Steroid dose was tapered gradually after the peritransplant period to 0.05 mg/kg within 6 months after surgery. Acute rejection (>1b or with hemodynamic compromise) was treated with a steroid bolus. Cytolytic therapy was added for repeated rejections or significant hemodynamic compromise. Endomyocardial biopsy was performed using the standard Stanford technique with either a Caves-Shultz or a disposable bioptome.[42] Biopsy-proven rejection was graded using the modified Billingham system adopted by the International Society for Heart and Lung Transplantation.[43].

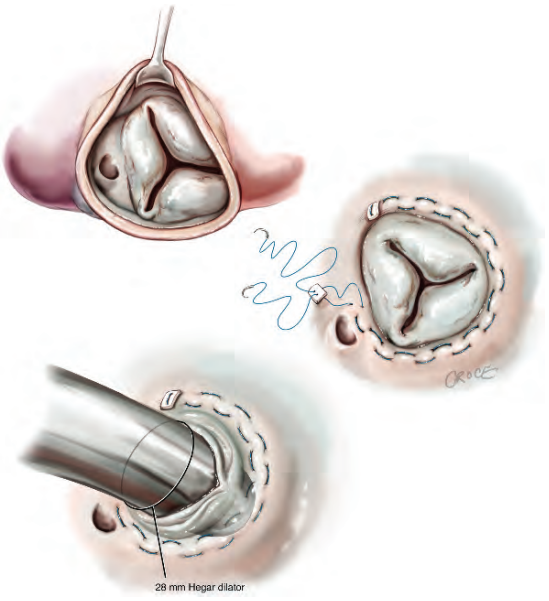


FIGURE 12.8. Tricuspid valve repair.

12.9.2.4. Echocardiographic Assessment of TR

Patients routinely underwent intraoperative transesophageal echocardiography (TEE), and then transthoracic echocardiography (TTE) studies at 1 week, 1 month, and then annually. As part of the echocardiographic studies, patients received two-dimensional and continuous-wave Doppler evaluation with color flow mapping. The tricuspid valve was examined in the parasternal short-axis and apical four-chamber views. Tricuspid regurgitation was graded by qualitative echocardiographic assessment according to the ratio of the regurgitant jet area to the right atrial area, as described previously. Grades of TR included 0, 1+ (jet to area ratio < 10%, trace), 2+ (ratio 10–24%, mild), 3+ (ratio 25–49%, moderate), and 4+ (ratio > 50%, severe). Multiple views were obtained and the regurgitation graded based upon the most abnormal views.

12.9.2.5. Hemodynamic Assessment

Intraoperative pulmonary artery monitoring with a Swan-Ganz catheter was performed in every patient. Right heart catheterization was routinely performed with biopsy at 1 week, 1 month, and annually, or if dictated by clinical condition. Intracardiac pressures were recorded at the levels of the right atrium, right ventricular body, and pulmonary artery. Thermodiluton cardiac outputs were also obtained.

12.9.2.6. Statistics

All numerical results are reported as mean ± standard deviation. A p value of less than 0.05 was considered to be significant. Statistical analysis

was performed using statistical package for the social sciences (SPSS) v.11 (SPSS Inc, Chicago, IL). Fisher's exact test was applied for associations of categorical variables, and the Wilcoxon rank sum test was used to compare means of continuous variables. Survival analysis was performed using the log rank statistic.

12.9.3. Results

General characteristics: There were 30 patients in each group. Recipient and donor demographics are presented in Tables 12.1 and 12.2, respectively. Pretransplant pulmonary artery pressures were similar in both groups (standard (STD) vs. TVA, p = ns: mPAP 28.6 ± 9.2 vs. 29.3 ± 8.9; pulmonary capillary wedge pressure (PCWP) 23.2 ± 8.9 vs. 23.8 ± 9.0; PVR Woods units 2.3 ± 0.9 vs. 2.1 ± 1.1). The two surgeons who performed the procedures were randomly distributed among the procurement and implantation groups, based on the call schedule. Both groups followed the same routine myocardial biopsy schedule. The average number of biopsies for the first year in survivors of both groups was 15.2. After the first year, patients received routine biopsies biannually unless clinically indicated. None of the patients required a permanent pacemaker. There was no incidence of tricuspid stenosis.

Tricuspid regurgitation: The average amount of TR in each group was stable during the study period. TEE evaluation of patients after weaning from CPB and stabilization revealed more TR in group STD (Table 12.3). The difference in average TR persisted at 1 and 6 years. Moreover, the standard group had a greater incidence of ≥2+ TR. Subsequently, there was a progressive increase in the number of patients with grade ≥3+ TR in group STD. Group TVA had a stable distribution of TR severity. No patients in group TVA developed significant TR (≥2+). By 6 years, three patients in group STD demonstrated clinical signs of TR with peripheral edema and increased diuretic requirements. Two required a tricuspid valve procedure. There was a significant correlation between ≥ 2+ TR and mortality as well as between TR and increase in creatinine level.

Hemodynamics: The hemodynamic values (Table 12.4) at 1 and 6 years were similar.

Renal function: The BUN was similar in the two groups. The baseline creatinine in group TVA seems higher in group STD (1.34 ± 0.67 vs. 1.02 ± 0.29), but it fails to attain significance. The serum creatinine increased in both groups after transplant, and continued to increase in group STD while stabilizing in

DropBooks

Table 12.1. Recipient demographics.

Group	Age	M/F	Height (cm)	Weight (kg)	Cause	UNOS	Mech	Reop
Standard (STD)	53.1 ± 12.2	18/12	169.2 ± 12.7	80 ± 12.7	Ish 13 Idio 16 PP 1	I 27 II 3	5	12
Tricuspid valve annuloplasty (TVA)	51.1 ± 11.7	20/10	172.2 ± 10.7	79.5 ± 18.7	Ish 13 Idio 17 PP 0	I 26 II 4	5	13
	ns	ns	ns	ns			ns	ns

M/F: male/female; Cause: *Ish* ischemic, *Idio* idiopathic, *PP* postpartum; UNOS: United Network of Organ Sharing listing status; Mech: mechanical assistance including LVAD or IABP; Reop: previous sternotomy.

Table 12.2. Donor demographics.

Group	Age	M/F	Height (cm)	Weight (kg)	D/R ratio
STD	26 ± 13.1	22/8	161 ± 35.9	65 ± 19.5	0.8 ± 0.2
TVA	26.9 ± 12.6	19/11	167.5 ± 16.2	67.5 ± 19.5	0.8 ± 0.2
	Ns	ns	ns	ns	ns

D/R ratio: ratio of donor/recipient weight.

Table 12.3. Distribution of the severity tricuspid regurgitation.

	Group	Average	≤1	2	≥3	% ≥2	% ≥3
Intraoperative	STD	1.1 ± 1.0	21	5	4	30.0	13.3
	TVA	0.33 ± 0.38	30	0	0	0.0	0.0
		$p = 0.01$				$p = 0.01$	$p = 0.002$
1 year	STD	1.3 ± 1.0	17	7	2	34.6	7.6
	TVA	0.2 ± 0.3	27	0	0	0.0	0.0
		$p = 0.01$				$p = 0.02$	$p = 0.01$
6 year	STD	1.5 ± 1.3	15	2	5	31.8	22.7
	TVA	0.5 ± 0.4	22	0	0	0.0	0.0
		$p = 0.01$				$p = 0.01$	$p = 0.005$

Table 12.4. Hemodynamic measurements.

	Group	mSys	mPA	CVP	mPA-CVP	CI
1 year	STD	82.1 ± 10.7	19.1 ± 9.2	6.5 ± 4.3	13.4 ± 6.5	3.6 ± 0.7
	TVA	87.3 ± 9.8	20.4 ± 9.1	6.9 ± 4.9	14.3 ± 6.32	3.3 ± 0.6
			ns	ns	ns	ns
6 year	STD	84.2 ± 12.1	23 ± 5.2	4.4 ± 3.2	15 ± 3.2	2.8 ± 0.5
	TVA	82.6 ± 11.8	22.2 ± 6.7	7.8 ± 4.4	14.5 ± 4.2	2.9 ± 0.5
		ns	ns	ns	ns	ns

mSys (mmHg): mean systemic blood pressure; mPA (mmHg): mean pulmonary artery pressure; CVP (mmHg): central venous pressure; CI (L/min/m^2): cardiac index.

Table 12.5. Renal function following heart transplantation.

	Group	BUN	Crt	dCrt
Preoperative	STD	22.3 ± 11.5	1.02 ± 0.3	
	TVA	26.8 ± 15.6	1.34 ± 0.7	
		ns	$p = 0.058$	
1 year	STD	42.5 ± 16.5	2.3 ± 1.3	1.3 ± 0.9
	TVA	37.7 ± 15	2.2 ± 1	1.0 ± 0.9
		ns	ns	$p = 0.061$
6 year	STD	41.0 ± 14.4	2.9 ± 2.0	2.0 ± 2.1
	TVA	32.1 ± 12.1	1.8 ± 0.7	0.7 ± 0.8
		ns	$p = 0.01$	$p = 0.005$

BUN (mg/dl): blood urea nitrogen; Crt (mg/dl): serum creatinine; dCrt: difference in creatinine from baseline.

group TVA. Serum creatinine and the difference in creatinine from baseline were significantly higher in group STD at 6 years (Table 12.5). In the overall population of patients, there was a correlation between creatinine level of ≥2+ and mortality (Figure 12.3).

Morbidity and mortality: Overall survival among both groups was similar with eight patients expiring in both groups. Group STD had a higher intraoperative mortality (4/30 vs. 0/30). Three deaths were due primarily to right heart failure and one to an acute rejection. Although the patients eventually died of multiple system organ failure, the root cause was low cardiac output. By the first and sixth years, survival was similar between groups (Table 12.6). Of note, seven of eight deaths in group STD were cardiac in origin. One patient died of a malignancy. In group TVA, there were three cardiac deaths, two perforated visceral organs, and three infections. There were statistically more cardiac-related deaths in group STD ($p < 0.05$). The average number of treated rejection episodes per patient was similar between groups.

12.9.4. Comment

Tricuspid regurgitation frequently develops following OHT and can be progressive. Variability exists between the common techniques for measuring TR. The color Doppler quantification method is the one used in this study and is the technique that is most widely accepted. Using this technique, Huddleston et al. found that 21% had greater than moderate TR. Williams et al. found a 32% prevalence of moderate to severe TR following heart transplantation.[44] Aziz et al. found that 36% of patients developed greater than moderate TR after OHT. In the largest study to date, the Stanford group analyzed 336 patients and found 34% had greater than moderate TR. In addition, the studies that follow patients over a period of time demon-

TABLE 12.6. Complications and mortality following heart transplantation.

		Mortality		
Group	Intraoperative complications	1 year	6 year	Cardiac deaths
A	Bleeding 3 Pul HTN/RHF 5 CVA 1 Pulm hem 1 Donor dys 2	RHF 3 Rejection 1	CHF 3 Cancer 1	7
B	Bleeding 3 Pul HTN/RHF 4 Donor dys 3	1 rejection 1 sepsis 1 pneumonia ns	CHF 2 Perforated bowel 2 Pneumonia 1 ns	3 $p = 0.03$

Pul HTN: pulmonary hypertension; RHF: right heart failure; CVA: cerebral vascular accident; Pulm hem: pulmonary hemorrhage; Donor dys: biventricular donor dysfunction; CHF: allograft failure.

strate the progressive nature of this abnormality. For instance, in the Stanford experience, the incidence of severe TR increases in survivors from 7.8% at 5 years to 14.2% at 10 years.

TR can become a serious condition. If the TR progresses past moderate, a majority of patients can develop peripheral edema, ascites, and renal dysfunction. Furthermore, the long-term survival in patients with moderate TR is decreased when compared to patients with less than mild TR. In a study analyzing intraoperative echocardiograms, immediate significant TR was associated with a poor long-term survival. The authors suggest a role for concomitant TVA at the time of transplant.

When severe TR is present, repair with an annuloplasty or replacement has been reported.[45] DeVega tricuspid annuloplasty is an inexpensive, quick, and stable method to reduce a dilated annulus. It has been primarily used to treat functional TR caused by elevated left-sided pressures with excellent long-term results. This study defined the role of prophylactic TVA. Whether the TVA is best accomplished by a DeVega technique or by a ring is based on surgeon's preference. Stabilization with an annuloplasty ring is preferable in patients with severe TR and dilatation of the annulus. However, in this study, none of the patients had an abnormally dilated annulus. The DeVega annuloplasty was performed to maintain the normal size of the annulus. This was clearly accomplished in the study as there was no progression or development of new TR in group TVA. The technique employed in the performance of the DeVega annuloplasty is important: careful and closely spaced sutures with a double pledgeted repair are critical in maintaining the integrity of the annulus. We have used an annuloplasty ring in other patients but have found the bulky prosthetic material to be a hindrance for biopsies, which makes these procedures time consuming and expensive. Complications of the TVA are uncommon, and are primarily related to injury of the conduction system. It is also important not to create stenosis by reducing the annulus excessively. Tricuspid stenosis or heart block did not occur in any patient.

TR following OHT is often a complication of the endomyocardial biopsy procedure.[46,47] Many studies correlate the presence of flail leaflets and torn chordae with severe TR. In fact, almost all reported cases of TV repair or replacement after OHT have demonstrated mechanical disruption of the TV. There is no reason to believe that a TVA would prevent mechanical disruption of the valve mechanism. However, since the annulus is decreased, TR from minor structural damage can be attenuated. Two patients in group TVA had biopsy-proven injury to the chordal structures. Subsequent echocardiograms confirmed ruptured chordae. However, the TR did not increase above a mild degree.

Other causes of TR have a functional basis. The presence of pulmonary hypertension may cause right ventricular and annular dilatation, causing TR. Pulmonary hypertension by itself with a normal RV appears to be well tolerated; superimposition of pulmonary injury or RV dysfunction may contribute

DropBooks

to a process leading to the development of TR. RV dysfunction can be caused in the intraoperative period by preservation or reperfusion injury, air embolus, donor risk factors, or accelerated rejection. The short-term results of this study demonstrated improved perioperative survival, especially when these stresses were imposed on a donor organ. Long term, there was a decrease in cardiac-associated mortality. If a cardiac-related stress is superimposed on a transplant patient, the TVA allows maintenance of myocardial efficiency, lower CVP, and perhaps enough restoration of perfusion to allow these patients to survive. However, OHT is associated with many factors that can cause death, such as infection and malignancy. Hence, despite being superior with regard to intraoperative and cardiac survival, the overall mortality in both groups was similar.

We exclusively used a bicaval technique for OHT. There is ample evidence that bicaval OHT is superior to standard biatrial OHT in preventing TR. This is attributed to elimination of the right atrium (RA)/(RV) relationship caused by the biatrial implantation technique. In a study of 249 patients, Aziz et al. report a 19.9% incidence of severe TR in the bOHT group as opposed to 51% for the sOHT group. Since there was evidence that bicaval OHT decreases TR and improves sinus node function[48,49] we used this technique for all patients. If the standard OHT technique had been utilized, the prophylactic TVA might theoretically be of additional benefit.

We tested the hypothesis that prophylactic TVA, done before OHT, could impact the incidence of TR, the need for further TV procedures, and patient outcomes.

The significant differences at long-term follow-up included prevention of significant TR and renal protection. The amount of TR was low, as would be expected from the bicaval technique, but was still different among the groups. In the early peritransplant period, group STD had a mean of 1.1 versus group TVA (0.33 TR). This is represented as a mean of only mild TR, but there was increased mortality in the patients who developed greater than moderate TR. Group TVA patients had only trivial TR; even the patients with myocardial dysfunction developed only mild TR. The difference in average TR continues to be present at 1 and 6 years of follow-up. Furthermore, in group STD, the percentage of patients with ≥2+ TR remained stable at ~30% throughout the study period. The incidence of moderate/severe TR (>3+) in group STD was 7.6% at 1 year and compares favorably to other reports using bOHT techniques. At 6 years, the severe TR group increased to 22.7% of the survivors. At 1 and 6 years, there were no patients with greater than mild TR in group TVA. Three patients in group STD developed clinical symptoms from central venous hypertension. Two required operative correction. It is evident from other reports that TR is progressive and can lead to worsening right heart failure symptoms. That is consistent with the STD group in this study. Furthermore, follow-up of patients in this study demonstrates that a TVA prevents development and progression of TR.

The other parameter that we studied was renal function, since there are data to correlate renal dysfunction with worsening TR. Increased CVP in patients with TR contributes to increased renal venous pressure, which has been shown to be responsible for decreased renal artery flow. This in turn increases plasma rennin activity, causes urinary protein leak, and decreases glomerular filtration rate. This explains the deterioration in renal function in patients with significant TR. In this study, patients' serum creatinine progressively increased during the first year in both groups. However, by 6 years, there was stabilization of renal function in group TVA and the different average levels of serum creatinine and the difference from baseline from group STD were significant. Furthermore, there was significant correlation between development of increased creatinine and mortality. Calcineurin inhibitors can contribute to renal dysfunction and that effect was present in both groups. However, the development of TR is an added insult and correlates with renal dysfunction. This effect is evident only after long-term follow-up and the development of moderate TR with deterioration in renal function.

In summary, this is the first long-term report of using prophylactic TVA to decrease TR after OHT. Previous reports using this patient population demonstrated survival benefit to TVA in the immediate postoperative period. This is the period when the heart is maximally stressed and the patients are vulnerable to the effects of a low perfusion state. This cardiac protective effect is present long term as demonstrated by less car-

diac-related deaths. However, the overall survival is similar. The study also demonstrates significant reduction in the mean severity and number of patients with significant TR. This prevention of TR has important long-term beneficial effect as the presence of moderate TR is progressive and associate with a poor prognosis. Since there is correlation between development of TR and renal dysfunction, the TVA helps preserve renal function. Prophylactic DeVega TVA is inexpensive, quick to perform, and durable at 1 year, and offers a survival advantage in the immediate postoperative period. Long term, there is better preservation of renal function and prevention of TR. Since TVA is beneficial, it should be routinely considered during preparation of a donor heart for transplantation.

12.10. High Thoracic Epidural Anesthesia

12.10.1. High Thoracic Epidural Analgesia

High thoracic epidural analgesia (HTEA) for cardiac surgery is a regional anesthetic technique that has been used selectively by a few institutions in the USA that are comfortable with its use. HTEA is routine in European countries, India, and Turkey. Epidural anesthesia can be associated with a small risk of an epidural hematoma theoretically calculated at a minimum of 1:150,000; this has precluded its widespread adoption in the USA.[50]

The use of neural sympathetic blockade for cardiac surgery is only in its second decade. At the Society of Cardiovascular Anesthesiologist meeting in 1995, Goldstein et al. presented their national survey results in the use of spinal and epidural techniques during cardiac surgery. The survey revealed that only 7% of responding anesthesiologists (24%) used this technique.[51]

Modulation of the cardiac sympathetics has been discussed extensively in the literature by several groups all of whom have noted similar findings. Cardiac neural blockade is noted to be associated with a decrease in the incidence of intra- and postoperative ischemia, a decrease in active postoperative warming, shortened extubation times (as short as 1.6 ± 0.5 h), an increase in the use of inotropes, a decrease in the use of agents for hypertension, and improved ventilatory parameters postoperatively. Cardiac and stroke index, as well as oxygen delivery, were significantly higher in the thoracic epidural group.[52–54] The primary pathophysiologic response to sympathetic stimulation differs in normal and atherosclerotic vessels. HTEA blunts the usual vasoconstriction in abnormal vessels.

The Liem group published its results in three separate papers.[52–54] A group of 27 patients received an epidural catheter at least 20 h prior to surgery. The catheter was inserted at the first or second thoracic interspace. It was injected initially with a solution of 0.375% bupivacaine and sufentanil 5 µg/ml in a dose of 0.05 ml/cm body length. A continuous infusion was initiated with 0.125% bupivacaine and sufentanil 1 µg/ml for surgery. Heart rate and mean arterial pressure decreased with the onset of the TEA bolus but stroke volume increased. Throughout the remainder of the anesthetic period, the TEA group maintained greater hemodynamic stability as evidenced by less hypotension, hypertension, and ischemia.

Postoperative outcomes in patients in the epidural group were that they awakened earlier (148 min vs. 335 min), resumed spontaneous ventilation earlier (326 min vs. 982 min), and were extubated sooner (463 min vs. 1140 min). This was accompanied by a significantly better visual analog pain score, sedation score, and postoperative Pao_2. The incidence of tachycardia (heart rate > 100 beats/min for >30 min) and ischemia was significantly lower in the thoracic epidural compared to the control group.

In the final section of Liem's study, adrenergic responses were contrasted. In the precardiopulmonary bypass period, there was less variability in systemic vascular resistance, heart rate, and mean arterial pressure, which were accompanied by smaller variations in plasma norepinephrine in the epidural group. During cardiopulmonary bypass, thoracic epidural anesthesia was associated with lower plasma norepinephrine levels and less variability in plasma epinephrine levels, although cortisol levels were increased.

In the postcardiopulmonary period, mean arterial pressure and systemic vascular resistance were higher and heart rates lower in the thoracic epidural group. In the 48 h after surgery, lower pain scores were correlated with lower epinephrine and plasma cortisol levels. Although Liem's group had

DropBooks

an increased systemic vascular resistance (SVR), a review of our thrombo-endarterectomy (TEA) patients with an epidural placed at T1–T2 demonstrated a 200–400 dynes/s average decrease in SVR when compared to patients without epidurals. X-ray with dye confirmation of catheters is standard for us; thus, they were not malpositioned. The difference may be due to our high-risk population of patients who were on a multitude of cardiac drugs immediately pre-op, such as ACE-inhibitors, and often had low EF or heart failure, all of which contributes to post-op hypotension. Unlike low thoracic and lumbar epidurals, which cause significant vasodilatation of the splanchnic bed and/or lumbar plexus, HTEA at T1/2 causes dilation of the intercostal arteries and pulmonary arteries. This along with our use of high concentrations with small volume infusion contributes very little to hypotension.[55,56] In our experience of 325 patients, we were most impressed with elderly patients who benefit significantly from HTEA. We noted a significant reduction in post-op delirium and confusion, very limited use of post-op narcotics, and observational decrease of post-op depression. As already studied, patients with TEA have a greater pulmonary effort, thus increasing TV and may shorten the recovery time of the post-op diaphragmatic muscle paralysis. This once again is particularly important in the elderly population prone to post-op pneumonia and atelectasis.[57]

The Kimo study examined a group of ten patients undergoing CABG surgery.[7] The use of thoracic epidural anesthesia as an adjuvant to a standard fentanyl-N_2O anesthetic reduced all measures of sympathetic activation in the myocardium. At the time of sternotomy, cardiac norepinephrine spillover, mean arterial pressure, systemic vascular resistance, and pulmonary capillary wedge pressure were all significantly increased in the control group. Although none of the patients in the TEA group had signs of myocardial ischemia, three of the ten control patients did. The patients, who underwent an examination of myocardial blood flow showed that regional myocardial oxygen consumption was lower in patients undergoing regional anesthesia. Both serum and greater cardiac vein concentrations of norepinephrine were lower in patients receiving epidurals around the time of sternotomy and were also significantly lower during cardiopulmonary bypass. As expected all groups demonstrated improved pain relief with thoracic epidural anesthesia with or without an opiate added.

Preliminary review of our 325 patients reveals a <2% incidence of post-op ischemia and no post-op MIs. Of interest, we were able to successfully use the Khuri myocardial pH probe in three of five HTEA patients. The anesthetic was stabilized and the epidural dosed with 4–5 cm^3 of 0.5% bupivacaine. Two patients had technical problems with placement and maintaining probe position. The successful three were monitored while the surgeons were preparing for bypass; thus there was no heart manipulation involved. During this period all patients revealed an increase in myocardial pH from the 6.9–7.1 range to 7.3–7.5 range without drug or mechanical manipulation over a period of 15–20 min. This is of extreme interest and parallels data by other investigators.

An interesting question to pursue in these patients would be "Does HTEA analgesia effect long-term outcomes?" The Anesthesia Patient Safety Foundation (September 2004) convened a panel of experts from anesthesia, surgery, cardiology, epidemiology, immunology, and administrative agencies to discuss issues related to long-term postoperative outcomes. It was proposed that inflammatory/immune response may be a potential biological link to long-term outcomes via contribution to disease acceleration. Also very preliminary data suggest that depth of anesthesia may be a predictor of outcome. Should this research prove correct then epidural anesthesia could reduce postoperative mortality and morbidity by allowing lighter general anesthesia and decreasing mediators of the inflammatory responses? As previously stated, the primary deterrent for routine use of TEA is the possibility of epidural hematoma formation. Once present, there is a limited window of 8–10 h in which spinal cord decompression must take place. There seems little logical reason to believe that a hole in an epidural vein (even the size of a 17-gauge Touhy needle) would lead to a sufficiently large hematoma to result in symptoms. The rate and amount of fluid flow are directly proportional to the pressure difference between the two areas of interest (ignoring for now the question of whether this flow is turbulent or laminar). In the case of a venous epidural hematoma, this pressure differential is the epidural venous system and the epidural space. The pressure inside the epidural veins is

roughly equivalent to the CVP (barring anatomical obstructions) while that of the epidural space is roughly equivalent to the cerebrospinal fluid pressure.[58–60] The "negative" pressure, which is commonly used as the marker for the space, is partially an artifact of the method used to enter the epidural space. As the dural ligament is pushed toward the subarachnoid membrane by the blunt Touhy needle, positive pressure is applied to the space. Once the ligament is penetrated, the ligament retracts and creates a brief but significant drop in pressure within the space (Figure 12.9, Okutomi et al.[60]).

The difference between these two pressures is minimal (usually 2–3 mmHg). Thus the rate of flow is slow and the volume which will enter the space does so only until the pressure in the epidural space rises to meet that of the veins. At that point, flow into the space will cease (in fact, if the pressure rises much higher than venous pressure, the veins will collapse). Thus, our group (J Williams) believes it is improbable that venous tears in the epidural space (in absence of anatomical aberrancy) will lead to neuroaxial trauma regardless of the state or type of heparinization. This is probably the reason epidural hematomas are so rare.[16]

How then to explain this rare but devastating complication? Our group (JPW) believes that the risk is entirely explained by the presence of rare but significant *arteri* vessels in the midline of the posterior epidural space. There are no quantitative studies documenting the ratio of venous to arterial vessels in the epidural space; however, the tenuous nature of the arterial blood supply to the spinal cord suggested that there are few, if any, posteriorly penetrating arterial vessels in the thoracic region. Further, in order to lead to neuroaxial trauma, the hematoma must exert enough pressure to compromise this tenuous blood supply. If one assumes that the arterial pressure to most of the cord is 45 mmHg, then pressure in the epidural space must reach this critical level in order to significantly impair sustenance to the neuraxis. It seems logical that if a hematoma with sufficient pressure to damage the neuraxis is present, arterial trauma is the culprit. It is with this thought in mind that our group analyzes blood withdrawn from an epidural needle or catheter for oxygen tension. If the oxygen tension is within 10% of a simultaneously obtained arterial blood sample, we recommend cancellation of the case and close observation for the next 12 h. If the oxygen tension is less than this, we continue the case, but choose an alternate insertion site. Using this method, we have noticed no hematomas in our first 200 patients; however, we have withdrawn venous blood on at least five occasions.[61]

Despite this eloquent hypothesis, most institutions proceed in a slightly different manner. We place all of our catheters the day before because nearly all of our patients are high risk and often are on anticoagulation therapy prior to surgery. Placement is usually done via fluoroscopy and contrast confirmation with neurological checks every 2 h overnight in a 23 -h observation period. We do not delay the case if blood is drawn back. Another site is attempted though. We only use Flex-tip plus catheters (Arrow) because their tips are blunt, and inject 5–10 cm^3 of saline prior to insertion of the catheter. The catheter is then tunneled for stabilization and infection control. Nearly one half of the reported epidural hematomas occur after the catheters are removed; thus all catheters are pulled when the coagulation profile correlates with American Society of Regional anesthesia and Pain Medicine (ASRA)

DropBooks

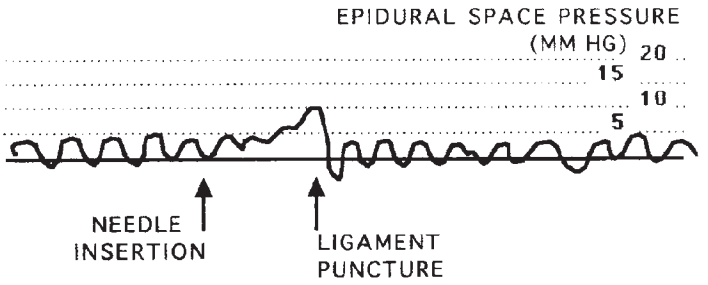


FIGURE 12.9. An example of a Touhy needle insertion in the thoracic epidural space. The oscillations in the waveform are respirations. Note that although there is a rapid descent once the ligament is penetrated, the pressure in the space rapidly returns to normal.

guidelines. Saline is also injected during the removal process. This has not been studied but is logical when avoidance of vessels is the main concern. Our recent review of 325 patients revealed no epidural hematomas or spinal trauma. This was despite the fact that over one half of the patients were on some form of anticoagulation preoperatively (discontinued prior to insertion) and 80% were on anticoagulation postoperately including heparin or enoxaparin with American Society of Anesthesiology (ASA). We feel that the small risk of a neuroaxial hematoma is outweighed by the benefits in patients with multiple comorbidities especially with a team experienced in managing high-risk epidurals. Close observation, well-informed and trained medical staff caring for the patient, and a well-educated patient are all key aspects of using this modality in a safe and successful manner.

12.11. Key Points to Remember

- A variety of enabling techniques have been utilized with great effect to allow better survival in the high risk heart failure population.
- Beating heart surgery is a simple technique that allows better preservation of both ventricles peri-operatively.
- Right heart failure is best treated by avoidance and pre-emption.
- Prophylactic plating of the sternum as an alternative to wire-closure is an effective way of improving sternal closure, thereby reducing the risk of deshiscence and mediastinitis in high risk patients.
- Tricuspid valve annuloplasty of the donor heart maybe an effective way of reducing tricuspid regurgitation, which can occur as a consequence of multiple interventions and rejection in transplanted patients.
- Sternal sparing incisions, where possible may reduce the bleeding and other morbidity related to sternotomy.
- High thoracic epidural anesthesia may be an extremely effective way of controlling pain post-operatively, in addition to reducing pulmonary artery pressures and improving myocardial perfusion theoretically.

References

1. Gummert JF, Barten MJ, Hans C, et al. Mediastinitis and cardiac surgery—An updated risk factor analysis in 10,373 consecutive adult patients. *Thorac Cardiovasc Surg*. 2002;50(2):385.
2. Krischak GD, Janousek A, Wolf S, Augat P, Kinzl L, Claes LE. Effects of one-plane and two-plane external fixation on sheep osteotomy healing and complications. *Clin Biomech*. 2002;17(6):470-476.
3. Dalton ML, Connally SR, Sealy WC. Julian's reintroduction of Milton's operation. *Ann Thorac Surg*. 1992;53(3):532-533.
4. Trumble DR, McGregor WE, Magovern JA. Validation of a bone analog model for studies of sternal closure. *Ann Thorac Surg*. 2002;74(3):739-744.
5. Song DH, Lohmann RF, Renucci JD, Jeevanandam V, Raman J. Primary sternal plating in high-risk patients prevents mediastinitis. *Eur J Cardiothorac Surg*. 2004;26:367-372.
6. Usry GH, Johnson L, Weems JJ Jr, Blackhurst D. Process improvement plan for the reduction of sternal surgical site infections among patients undergoing coronary artery bypass graft surgery. *Am J Infect Control*. 2002;30(7):434-436.
7. Tavilla G, van Son JA, Verhagen AF, Lacquet LK. Modified Robicsek technique for complicated sternal closure. *Ann Thorac Surg*. 1991;52(5):1179-1180.
8. Gottlieb LJ, Pielet RW, Karp RB, Krieger LM, Smith DJ, Deeb GM. Rigid internal fixation of the sternum in pos-operative mediastinitis. *Arch Surg*. 1994;129(5):489-493.
9. Grmoljez PF, Barner HH, Willman VL, Kaiser GC. Major complications of median sternotomy. *Am J Surg*. 1975;130(6):679-681.
10. Chase CW, Frankling JD, Guest DP, Barker DE. Internal fixation of the sternum in median sternotomy dehiscence. *Plast Reconstr Surg*. 1999;103(6):1667-1673.
11. Ogus TN, Hulusi UM, Cicek S, Ozkan S, Yuksel OO, Isik O. Sternal cyanoacrylate gluing in mediastinitis. Effects on infection, stability and bone healing. *J Cardiovasc Surg*. 2002;43(5):741-746.
12. Negri A, Manfredi J, Terrini A, et al. Prospective evaluation of a new sternal closure method with thermoreactive clips. *Eur J Cardiothorac Surg*. 2003;22(4):571-575.
13. Schnittger I, Appleton CP, Hatle LK, Popp RL. Diastolic mitral and tricuspid regurgitation by Doppler echocardiography in patients with atrioventricular block: New insight into the mechanism of atrioventricular valve closure. *J Am Coll Cardiol*. 1988;11(1):83-88.

14. Gibson TC, Davidson RC, DeSilvey DL. Presumptive tricuspid valve malfunction induced by a pacemaker lead: A case report and review of the literature. *Pacing Clin Electrophysiol*. 1980;3(1):88-95.
15. Coats AJ. MADIT II, the Multi-Center Autonomic Defibrillator Implantation Trial II stopped early for mortality reduction, has ICD therapy earned its evidence-based credentials? *Int J Cardiol*. 2002;82(1):1-5.
16. Zareba W, Piotrowicz K, McNitt S, Moss AJ; MADIT II Investigators. Implantable cardioverter-defibrillator efficacy in patients with heart failure and left ventricular dysfunction (from the MADIT II population). *Am J Cardiol*. 2005;95(12):1487-1491.
17. Sakai M, Ohkawa S, Ueda K, et al. Tricuspid regurgitation induced by transvenous right ventricular pacing: Echocardiographic and pathological observations [article in Japanese]. *J Cardiol*. 1987;17(2):311-320.
18. Filsoufi F, Anyanwu AC, Salzberg SP, Frankel T, Cohn LH, Adams DH. Long-term outcomes of tricuspid valve replacement in the current era. *Ann Thorac Surg*. 2005;80(3):845-850.
19. Morgan DE, Norman R, West RO, Burggraf G. Echocardiographic assessment of tricuspid regurgitation during ventricular demand pacing. *Am J Cardiol*. 1986;58(10):1025-1029.
20. Sanders GD, Hlatky MA, Owens DK. Cost-effectiveness of implantable cardioverter-defibrillators. *N Engl J Med*. 2005;353(14):1471-1480.
21. Lin G, Nishimura RA, Connolly HM, Dearani JA, Sundt TM 3rd, Hayes DL. Severe symptomatic tricuspid valve regurgitation due to permanent pacemaker or implantable cardioverter-defibrillator leads. *J Am Coll Cardiol*. 2005;45(10):1672-1675.
22. Chang BC, Lim SH, Yi G, et al. Long-term clinical results of tricuspid valve replacement. *Ann Thorac Surg*. 2006;81(4):1317-1323, discussion 1323-1324.
23. Molina JE, Benditt DG. An epicardial subxiphoid implantable defibrillator lead: Superior effectiveness after failure of standard implants. *Pacing Clin Electrophysiol*. 2004;27(11):1500-1506.
24. Higashidate M, Tamiya K, Kurosawa H, Imai Y. Role of the septal leaflet in tricuspid valve closure. Consideration for treatment of complete atrioventricular canal. *J Thorac Cardiovasc Surg*. 1992;104(5):1212-1217.
25. Fukuda S, Song JM, Gillinov AM, et al. Tricuspid valve tethering predicts residual tricuspid regurgitation after tricuspid annuloplasty. *Circulation*. 2005;111(8):975-979. Epub Feb 14, 2005.
26. Fukuda S, Gillinov AM, McCarthy PM, et al. Determinants of recurrent or residual functional tricuspid regurgitation after tricuspid annuloplasty. *Circulation*. 2006;114(1, suppl):I582-I587.
27. Alfieri O, De Bonis M, Lapenna E, Agricola E, Quarti A, Maisano F. The "clover technique" as a novel approach for correction of post-traumatic tricuspid regurgitation. *J Thorac Cardiovasc Surg*. 2003;126(1):75-79.
28. Sahar G, Stamler A, Erez E, et al. Etiological factors influencing the development of atrioventricular valve incompetence after heart transplantation. *Transplant Proc*. 1997;29:2675-2676.
29. Ichikawa S, Takeuchi Y, Suda Y, et al. Tricuspid valve replacement after cardiac transplantation. *JJTCVS*. 2000;48:659-662.
30. Huddleston C, Rosenbloom M, Goldstein J, et al. Biopsy-induced tricuspid regurgitation after cardiac transplantation. *Ann Thorac Surg*. 1994;57(4):832-836.
31. Lewen M, Bryg R, Miller L, et al. Tricuspid regurgitation by Doppler echocardiography after orthotopic cardiac transplantation. *Am J Cardiol*. 1987;59(15):1371-1374.
32. Chan M, Giannetti N, Kornbluth M, et al. Severe tricuspid regurgitation after heart transplantation. *J Heart Lung Transplant*. 2001;20:709-717.
33. Bainbridge A, Cave M, Roberts M. A prospective randomized trial of complete atrioventricular transplantation versus ventricular transplantation with atrioplasty. *J Heart Lung Transplant*. 1999;18:407-413.
34. Aziz T, Burgess M, Rahman A, et al. Risk factors for tricuspid valve regurgitation after orthotopic heart transplantation. *Ann Thorac Surg*. 1999;68(4):1247-1251.
35. Aziz T, Saad R, Burgess M, et al. Clinical significance of tricuspid valve dysfunction after orthotopic heart transplantation. *J Heart Lung Transplant*. 2002;21:1101-1108.
36. Anderson CA, Stanton SK, Leacche M, et al. Severity of intraoperative tricuspid regurgitation predicts poor late survival following cardiac transplantation. *Ann Thorac Surg*. 2004;78:1635-1643.
37. Cipullo R, Finger MA, Ponce F, et al. Renal failure as a determinant of mortality after cardiac transplantation. *Transplant Proc*. 2004;36:989-990.
38. Vossler MR, Ni H, Toy W, et al. Pre-operative renal function predicts development of chronic renal insufficiency after orthotopic heart transplantation. *J Heart Lung Transplant*. 2002;21:874-881.
39. Morishita A, Kitamura M, Noji S, et al. Long-term results after DeVega's tricuspid annuloplasty. *J Cardiovasc Surg (Torino)*. 2002;43(6):773-777.
40. Jeevanandam V, Russell H, Mather P, et al. A one-year comparison of prophylactic donor tricuspid annuloplasty in heart transplantation. *Ann Thorac Surg*. 2004;78(3):759-766.

DropBooks

41. Sarsam R, Campbell C, Yonan N, et al. An alternative surgical technique in orthotopic cardiac transplantation. *J Cardiovasc Surg*. 1993;8:344-349.
42. Caves P, Stinson E, Billingham M, et al. Percutaneous transvenous endomyocardial biopsy in human heart recipients: Experience with a new technique. *Ann Thorac Surg*. 1973;16(4):325-336.
43. Billingham M, Cary N, Hammond M, et al. A working formulation for standardization of nomenclature in the diagnosis of heart and lung rejection: Heart Rejection Study Group. The International Society for Heart Transplantation. *J Heart Transplant*. 1990; 9(6):587-593.
44. Williams M, Lee M, Disalvo T, et al. Biopsy-induced flail tricuspid leaflet and tricuspid regurgitation following orthotopic cardiac transplantation. *Am J Cardiol*. 1996;77(15):1339-1344.
45. Crumbley A III, Van Bakel A. Tricuspid valve repair for biopsy-induced regurgitation after cardiac transplantation. *Ann Thorac Surg*. 1994;58(4):1156-1160.
46. Braverman A, Coplen S, Mudge G, et al. Ruptured chordae tendineae of the tricuspid valve as a complication of endomyocardial biopsy in heart transplant patients. *Am J Cardiol*. 1990;66(1):111-113.
47. Tucker P II, Jin B, Gaos C, et al. Flail tricuspid leaflet after multiple biopsies following orthotopic heart transplantation: Echocardiographic and hemodynamic correlation. *J Heart Lung Transplant*. 1994;13(3): 466-472.
48. Brandt M, Harringer W, Hirt S, et al. Influence of bicaval anastamoses on late occurrence of atrial arrhythmia after heart transplantation. *Ann Thorac Surg*. 1997;64:70.
49. Rothman S, Jeevanandam V, Combs W, et al. Eliminating bradyarrhythmias after orthotopic heart transplantation. *Circulation*. 1996;94:278-282.
50. Ho AM, Chung DC, Joynt GM. Neuraxial blockade and hematoma in cardiac surgery: Estimating the risk of a rare adverse event that has not (yet) occurred. *Chest*. 2000;117:551-555.
51. Goldstein S, Dean D, Kim SJ, et al. A survey of spinal and epidural techniques in adult cardiac surgery. *J Cardiothorac Vasc Anesth*. 2001;2:158-168.
52. Liem TH, Booij LH Hasenbos MA, et al. Coronary artery bypass grafting using two different anesthetic techniques. Part one. Hemodynamic results. *J Cardiothorac Vasc Anesth*. 1992;6:148-155.
53. Liem TH, Hasenbos MA, Booij LH, et al. Coronary artery bypass grafting using two different anesthetic techniques. Part two. Postoperative outcomes. *J Cardiothorac Vasc Anesth*. 1992;6:156-161.
54. Liem TH, Booij LH, Gielen MJ, et al. Coronary artery bypass grafting using two different anesthetic techniques. Part three. Adrenergic responses. *J Cardiothorac Vasc Anesth*. 1992;6:162-167.
55. Magnusdottir H, Kirno K, Ricksten SE, et al. High thoracic epidural anesthesia does not inhibit sympathetic nerve activity in the lower extremities. *Anesthesia*. 1999;91(5):1299.
56. Dernedde M, Stadler M, Bardiau F, et al. Continuous epidural infusion of large concentration/small volumes versus small concentration/large volume of Levobupivacaine for post operative analgesia. *Anesth Analg*. 2003;96:79-801.
57. Stenseth R, Bjella L, Berg EM, et al. Effects of thoracic eidural analgesia on pulmonary function after coronary bypass surgery. *Eur J Cardiothorac Surg*. 1996;10:859-865.
58. Shah JL. Positive lumbar extradural space pressure. *Br J Anaesth*. 1994;73:309-315.
59. Hamada J-L, Fujioka S, Ushio Y. Clinical investigation of lumbar epidural pressure. *Neurosurgery*. 1993;32:780-784.
60. Okutomi T, Watanabe S, Goto F. Time course in thoracic epidural pressure measurement. *Can J Anaesth*. 1993;40:1044-1048.
61. Williams JP. Thoracic epidural Anesthesia for cardiac surgery: Refresher Course. *Can J Anesth*. 2002;49(6): R1-R6.

13
Catheter-Based and Surgical Therapy for Ventricular Tachycardia

Bradley P. Knight, J. Massen, Gil Bolotin, and Jai Raman

13.1. Catheter Ablation for Ventricular Tachycardia in Patients with Heart Failure

13.1.1. Ventricular Tachycardia Mechanisms and Indications for Catheter Ablation

The mechanism for sustained VT in most patients with heart failure is reentry, and the substrate is usually endocardial scar. This is especially true for heart failure patients with an ischemic cardiomyopathy. A figure of eight model of reentry is a useful concept when considering the reentrant VT circuit in patients with heart failure. The activation wave front emerges from a common channel or isthmus during VT and causes global ventricular activation. A QRS complex is generated during global activation. The wave front then travels in opposing directions as it spreads across the myocardium, and forms at least two outer loops, which each circulate around an obstacle. The wave fronts join and reenter the isthmus at the opposite end of the channel. After slowly traveling through the channel, the activation wave front emerges again from the isthmus to cause global activation. The reentrant circuit is completed. This results in a figure of eight pattern of activation and sustained monomorphic VT.

The obstacles around which the wave front travels are either anatomically determined, based on the presence of a scar or a boundary such as the mitral annulus, or functionally determined, based on abnormal areas of refractory tissue. The area of slow conduction that forms the isthmus is usually the narrowest part of the reentrant circuit, and because it is located usually within the subendocardial peri-infarct zone, can often be transected using an endocardial ablation approach.

Patients with heart failure and VT or ventricular fibrillation (VF) are usually treated with implantable cardioverter-defibrillator (ICD) therapy, which is discussed below. However, a subset of patients treated with an ICD receives an unacceptable number of therapies, despite treatment with antiarrhythmic drugs to suppress the VT. Catheter ablation is an effective treatment for patients with heart failure who have an ICD and medically refractory VT. Specific indications include frequent ICD shocks,[1] incessant VT, or VT that is relatively slow and falls below the programed cutoff rate of the ICD. The ideal candidate for VT ablation is a patient with recurrent monomorphic VT, which is of the same morphology each time and is hemodynamically tolerated. It is optimal that the VT is well tolerated so that the VT can be localized while the patient is in tachycardia. However, patients with unstable VT, or multiple VTs, can also be treated with ablation by the use of alternative techniques to identify the VT origin while the patient is in sinus rhythm.[2] Patients with recurrent polymorphic VT or VF are usually not suitable candidates for catheter ablation, although new techniques are emerging to ablate the triggers for VF in patients with VF storm post myocardial infarction.

13.1.2. Preparation

Prior to performing catheter ablation for recurrent VT in a patient with heart failure, it is important

DropBooks

that secondary causes of VT, such as ischemia, drug toxicity, electrolyte abnormalities, and significant volume overload, have been excluded. Many patients with frequent ICD shocks have several VTs that can be induced with programed stimulation during an electrophysiology procedure. During the ablation procedure, the focus should be to eliminate the VTs that are clinically relevant. Therefore, if it is feasible, a 12-lead electrocardiogram (ECG) should be recorded before the procedure while the patient is in tachycardia to identify the clinical VT. A 12-lead ECG is also of value when localizing the tachycardia origin. For patients who have an ICD, retrieval and printout of the intracardiac electrograms should also be completed to help determine the characteristics of the clinical tachycardia. Finally, to minimize the risk of thromboembolism, a left ventricular thrombus should be excluded using echocardiography.

Immediately before the ablation procedure, the ICD should be reprogramed to suspend therapies for VT so that the VT will be sustained and mappable after it is induced. Catheters are usually placed from the femoral vein for right atrial and ventricular pacing and recording. A transfemoral retrograde aortic approach is the preferred method for mapping the left ventricle. Many patients with an ischemic cardiomyopathy have severe peripheral arterial disease. In these patients, a long guiding sheath that extends above the iliac bifurcation is useful to help guide the ablation catheter retrograde through the arterial system. A transseptal approach can also be used as an alternative when arterial access cannot be achieved.

Standard radiofrequency current continues to be the most commonly used energy source for ablation of VT in patients with heart failure. A conventional 4-mm tip catheter is usually used for mapping and ablation; however, alternatives include the use of larger ablation electrodes and cooled-tip electrodes to create larger lesions.

13.1.3. Localization of Ventricular Tachycardia Circuit

The 12-lead ECG of the VT can be used to determine the general vicinity of the VT. In most patients with structural heart disease, the VT arises from the left ventricle. A right bundle branch block morphology in lead V1 is consistent with a left-free wall origin and a left bundle branch block morphology in lead V1 is consistent with a left septal origin. Rarely, a VT can arise from the right ventricle in a patient with a myopathy. The axis in the limb leads can distinguish a superior from an inferior origin and the precordial transition can help localize the origin in the apical-basal direction. The infarct location as identified using cardiac imaging can help direct one to the VT origin, but many patients with heart failure do not have a single, focal infarction. Patients with heart failure more commonly have an ischemic myopathy with diffuse scarring that results in VTs from several locations within the left ventricle.

Several techniques have been described to identify the critical part of the VT circuit during tachycardia for successful ablation. These techniques can be divided into observations made from the endocardial recordings during VT and those made at the time of pacing at the site of interest during the VT. Because the isthmus of the VT is commonly associated with very slow conduction, typical findings at recording sites within the circuit are middiastolic potentials and late systolic potentials. Often there is continuous electrical activity recorded when the ablation electrode is positioned within the VT circuit.

When pacing is performed within the protected isthmus during VT, the tachycardia is continuously reset. This results in acceleration of the tachycardia to the pacing rate and a QRS configuration that is identical to the VT. This is referred to as concealed entrainment. Pacing at a site near the exit from the common channel results in a short stimulus-to-QRS interval and pacing at a site near the entrance results in a long stimulus-to-QRS interval. When pacing is performed outside of the circuit, the tachycardia can be entrained, but because part of the myocardium will be depolarized from the pacing site there will be fusion evident on the ECG. Pacing sites that are associated with fusion are not successful target sites for ablation.

A majority of ablation attempts at sites associated with both concealed entrainment and a middiastolic potential are successful. Additional observations at sites associated with concealed entrainment have been reported to enhance the likelihood of successful ablation. These include a comparison of the interval from the pacing

stimulus to the QRS and the interval from the electrogram to the QRS, and a comparison of the postpacing interval at the pacing site to the tachycardia cycle length. Use of these maneuvers can theoretically distinguish the common pathway from a bystander pathway, but is limited by the common presence of near continuous signal recordings within the scar.[3]

13.1.4. Ablation for Hemodynamically Unstable Ventricular Tachycardia

Patients with heart failure often have recurrent VT that is too rapid to be hemodynamically tolerated. Conventional mapping techniques that are used to localize the VT during the tachycardia are not helpful in these patients. Occasionally, maneuvers can be performed to improve the tolerability of the VT, such as slowing the tachycardia with intravenous procainamide, elevating the blood pressure during VT with vasopressors, or performing the procedure with cardiopulmonary bypass, but this is often unsuccessful or is associated with significant risk. Therefore, techniques have been developed to localize the VT during sinus rhythm.

One approach is to use a noncontact advanced mapping system.[4] This involves placement of a small inflatable balloon covered with a multiple electrode array into the left ventricle. The array is placed in addition to the ablation catheter and is usually accomplished using a double retrograde aortic approach. The system records intracavitary potentials from the array that is floating in the left ventricle and calculates the morphology of the endocardial potentials. The virtual electrograms are displayed on a three-dimensional reconstruction of the left ventricular endocardium after the operator has delineated the endocardial border using the ablation catheter. The system can localize the ablation catheter in space and can be used to navigate the catheter nonfluoroscopically. The navigation aspect of the system can be used to create linear lesions using sequential focal delivery of radiofrequency current.[5] This approach allows the VT to be induced once, recorded, and terminated. While the patient is in sinus rhythm, the endocardial recordings obtained during the VT can be analyzed offline to define the activation wave front of the VT and to identify middiastolic potentials.

Another approach to ablation of hemodynamically unstable VT in patients with heart failure is the use of an electro-anatomic advanced mapping system to create a three-dimensional reconstruction of the left ventricle that displays areas of scar. Scar can be defined as endocardial sites that are associated with the absence of a sizable intracardiac electrogram. Pacing at sites along the border of the scar can also be used to localize VT exit sites, which are often associated with a paced QRS morphology that is similar to that of the VT. Several focal ablation lesions can be delivered in sequence to create linear lesions that connect scars to each other or to connect scars to anatomical barriers such as the mitral annulus, in an effort to transect critical sites required for maintenance of reentrant VT. The mapping system can be used to navigate the catheter and catalog the lesion set.

13.1.5. Epicardial Ablation

Endocardial catheter ablation for VT in patients with structural heart disease is associated with a success rate of ~70–80%. When ablation is unsuccessful, an epicardial location of the critical portion of the VT circuit should be considered.[6]

An epicardial location appears to be more common among patients with a nonischemic dilated cardiomyopathy. The pericardial space can be accessed using a percutaneous subxiphoid needle approach using fluoroscopic guidance and radiographic contrast, or surgically via a small subxiphoid window. The epicardial surface of the left ventricle can be mapped using a standard steerable ablation catheter and ablation targets can be selected based on recordings during the VT and pacing maneuvers. It is important to visualize the coronary arteries before delivery of radiofrequency current to avoid coronary injury.

We have had experience in this area of intervention with a hybrid approach, with the surgeons providing access through the subxiphoid approach in the electrophysiology lab. The pericardial space is then visualized with the aid of a thoracoscope and the ablation carried out safely. This is an area of ongoing collaboration between cardiac electrophysiologists and cardiac surgeons (Figure 13.1).

DropBooks

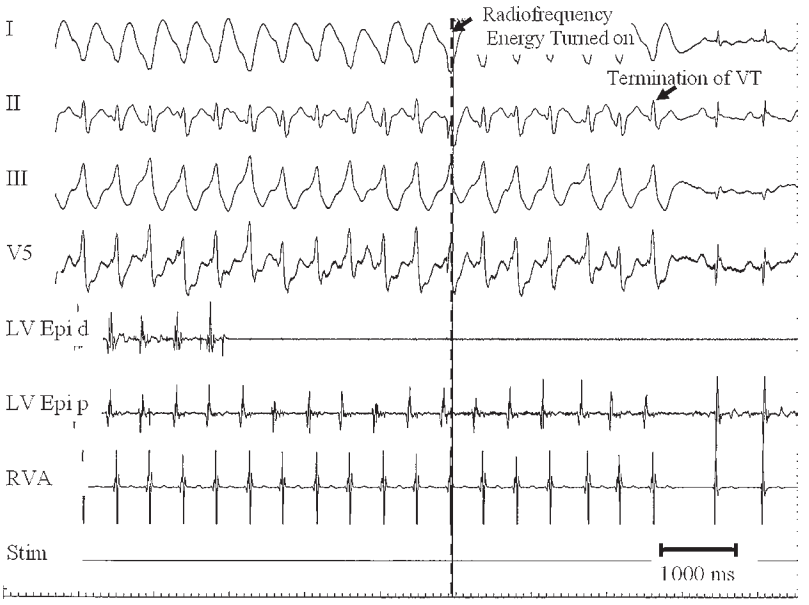


FIGURE 13.1. Termination of ventricular tachycardia (VT) during a catheter ablation procedure. The patient had a nonischemic dilated cardiomyopathy with recurrent monomorphic VT that could not be ablated using an endocardial approach. Access to the pericardial space was obtained using a subxiphoid window by a cardiac surgeon. Ablation was successful using a standard ablation electrode catheter placed in the pericardial space. The VT terminated within a few seconds after radiofrequency current was delivered to the epicardium at a critical portion of the reentrant circuit.

13.2. Surgical Therapy for Ventricular Tachycardia

Surgical therapy for ventricular arrhythmias was an important cornerstone of arrhythmia surgery in the mid-1980s. However, these procedures fell into disuse when performed in isolation. Currently, left ventricular reconstruction is often performed in association with endocardial radiofrequency ablation of the border zone to eradicate the VT foci. Widespread use of automatic implantable cardioverter defibrillators (ICDs) in patients with low ejection fractions may help in preventing postoperative arrhythmias, while the substrate is addressed by the reduction in ventricular size and exclusion of the scarred segments. However, in the developing world, where cardiac surgery is on the ascendance, more procedures are being performed for heart failure. In patients undergoing left ventricular reconstruction, we would strongly recommend ablating the border zone of the scarred segments with medium power electrocautery. In our own experience, we have used radiofrequency ablation (both unipolar and fluid-cooled unipolar devices) as well as cryo-ablation, with encouraging results. A common trap in patients with scarred ventricles with more than one scar can be that while addressing the largest scar, the other scars that are not hemodynamically significant or obvious are left alone. One of these smaller scars may then act as a focus for initiation of ventricular tachyarrhythmias. It may be prudent to treat these patients prophylactically with amiodarone.

Key Points to Remember

- Ventricular dysfunction is associated with an increased risk of ventricular arrhythmias, which may be a cause of sudden death.
- Catheter ablation of ventricular tachycardia may be effective for discrete scars that cause lethal ventricular rhythms.
- Surgical ablation is usually performed along with left ventricular reconstructions of large confluent scars.
- Implantable cardioverter-defibrillators are indicated for primary prevention in patients with poor ventricular function.

References

1. Strickberger SA, Man KC, Daoud E, et al. A prospective evaluation of catheter ablation of ventricular tachycardia as adjuvant therapy in patients with coronary artery disease and an implantable cardioverter/defibrillator. *Circulation*. 1997;96:1525-1531.
2. Soejima K, Suzuki M, Maisel WH, et al. Catheter ablation in patients with multiple and unstable ventricular tachycardias after myocardial infarction: Short ablation lines guided by reentry circuit isthmuses and sinus rhythm mapping. *Circulation*. 2001;104:664-669.
3. Bogun F, Knight BP, Goyal R, Strickberger SA, Hohnloser SH, Morady F. Clinical value of the postpacing interval for mapping of ventricular tachycardia in patients with prior myocardial infarction. *J Cardiovasc Electrophysiol*. 1999;10:43-51.
4. Strickberger SA, Knight BP, Michaud GF, Pelosi F, Morady F. Mapping and ablation of ventricular electrograms using a noncontact, computerized mapping system. *J Am Coll Cardiol*. 2000;35:414-421.
5. Knight BP, Bogner P, Wasmer K, et al. Human pathological validation of left ventricular linear lesion formation guided by noncontact mapping. *J Cardiovasc Electrophysiol*. 2002;13:79-82.
6. Aseem DD, Burke MC, Hong TE, Kim S, Salem Y, Knight BP. Termination of epicardial left ventricular tachycardia by pacing without global capture. *J Cardiovasc Electrophysiol*. 2005;16:92-94.

DropBooks

14
Catheter Ablation for Atrial Fibrillation in Patients with Heart Failure

Bradley P. Knight

14.1. Background

Pharmacologic therapy for atrial fibrillation (AF) is limited in patients with congestive heart failure (CHF), because the antiarrhythmic effect of most drugs is not specific for the atrium and is associated with ventricular proarrhythmia in patients with ventricular dysfunction.

Several nonpharmacologic therapies have been developed to treat AF in patients with CHF. For patients in whom sinus rhythm cannot be maintained, and the ventricular rate cannot be controlled, catheter ablation or modification of the atrioventricular junction has been shown to improve symptoms and often improves ventricular function.[1] The advantages of modification of the atrioventricular node over complete ablation include cost savings, and minimization of pacemaker dependency and the adverse hemodynamic effects associated with right-ventricular pacing. However, complete ablation and pacemaker implantation is more commonly performed, because it is more definitive and eliminates the irregularity of the ventricular rhythm.

Nonpharmacologic options for rhythm control include catheter ablation. Many catheter-based approaches have been proposed. However, most of the experience with catheter ablation for AF has not been in patients with CHF, but has targeted patients with AF and minimal structural heart disease.

14.2. Percutaneous Endocardial Maze Procedure

The first strategies at catheter ablation to cure AF represented attempts to replicate the surgical maze procedure using an endocardial catheter approach. Early experience by Schwartz showed that AF could in fact be cured by using a standard ablation catheter to deliver sequential confluent focal lesions with radiofrequency (RF) energy to create linear atrial lesions. More advanced catheter designs including a deployable loop catheter were developed in an attempt to improve the ability to create reliable, contiguous, transmural linear lesions. The MECA (Multiple Electrode Catheter Ablation) trial was designed to determine the safety and feasibility of specially designed catheters with multiple large electrodes used to create circular, biatrial linear endocardial lesions to treat AF.[2] The concept and catheter design were based on encouraging animal data. However, the MECA study was terminated prematurely because of a relatively high complication rate and low efficacy rate. Additional limitations of a percutaneous Maze procedure include a long, technically difficult procedure and the risk of causing atrial tachycardias because of conduction gaps in the ablation lines. The role of linear atrial lesions in the treatment of AF remains unresolved.

14.3. Focal Ablation

Haissaguerre and colleagues published a revolutionary observation in 1998 that the atrial muscle sleeves that extend over the pulmonary veins (PVs) are an important source of ectopic beats capable of triggering AF.[3] The PV muscle sleeves also appear to provide the conditions necessary to maintain reentry and perpetuation of AF. Based on these observations, attempts were made to cure paroxysmal AF by ablating the initiating, ectopic foci that arose from within the PVs. The limitations of this focal approach include the presence of multiple PV foci, a paucity of spontaneous or inducible AF during the procedure, the subsequent development of new foci, and the difficulty in mapping triggers when AF is persistent. In addition, delivery of RF energy deep within the PV can lead to PV stenosis.

14.4. Segmental Ostial Pulmonary Vein Isolation

Electrical isolation of the PVs avoids many of the limitations of focal PV ablation. By isolating a PV from the atrium without ablating the entire circumference of the PV ostium, Haissaguerre and his group developed a technique referred to as segmental ostial catheter ablation (SOCA).[4] The myocardial sleeves that connect the PV to the left atrium are a complex network of fibers. These fibers do not completely encircle the venous os, but are typically located in segments or quadrants and spiral around the vein. Electrophysiological mapping can be performed to identify the site of earliest PV muscle activation at the ostium and the PV can be electrically disconnected by delivering RF energy to sectors around the PV ostium without ablating around the entire circumference.

The SOCA procedure involves transseptal catheterization and placement of a standard ablation catheter and a circular electrode mapping catheter into the left atrium. The mapping catheter is positioned near the ostium of the PV and used to identify the site of earliest PV activation. The ablation catheter is moved toward the target site found using the mapping catheter and ablation is performed. After ablation is performed at the site of earliest activation, the activation sequence usually changes and the next target is identified. Ablation is continued until there are not more ostial PV electrograms recordable. Initial strategies consisted of ablating only the arrhythmogenic PVs, but empiric isolation of all four PVs has been shown to be associated with a higher success rate. Venography of the PVs and intracardiac echocardiography are commonly used to guide ablation and to avoid delivery of RF current in the PVs (Figure 14.1).

The SOCA has been associated with high success rates in patients with paroxysmal AF and minimal underlying heart disease. The low success rate at most centers in patients with heart failure could be explained by marked abnormalities of the remaining atrial tissue in patients with CHF. It seems that only electrical isolation of the PV would not eliminate the substrate for AF in patients with CHF. Despite the experience of other centers, the Haissaguerre group recently published a high success rate in patients with CHF using the SOCA technique. They performed SOCA in 58 patients with AF who also had CHF and left ventricular ejection fraction (LVEF) of <45%.[5] Half of the patients required two ablation procedures, and additional left atrial linear ablation was performed in some patients. The authors found that 78% of patients were in sinus rhythm after 1 year and that restoration and maintenance of sinus rhythm by catheter ablation significantly improved cardiac function, symptoms, exercise capacity, and quality of life.

14.5. Circumferential Ablation

A more recent left atrial (LA) endocardial ablation technique has been described by Pappone and adopted by many centers to treat AF.[6] This technique uses a circumferential ablation approach that targets the tissue that is on the atrial side of the LA–PV junction. Theoretically, this approach eliminates the triggers and the substrate that are missed using the SOCA approach and are unlikely to cause PV stenosis because the energy is delivered several millimeters away from the ostium of the veins. This procedure is commonly performed using a single, standard ablation catheter in the left atrium and a 3-D electroanatomic mapping system to map the atria and PVs. A randomized comparison of the SOCA and left atrical catheter ablation (LACA) approaches

DropBooks

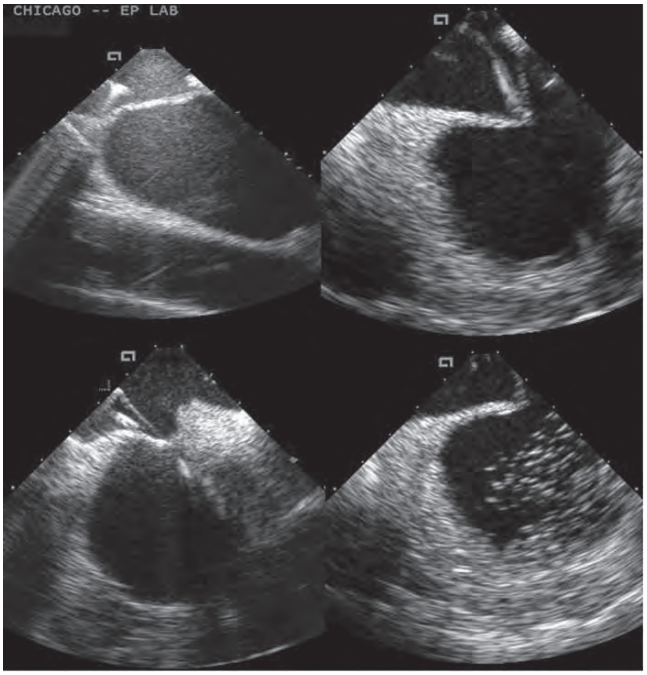


FIGURE 14.1. Example of the use of phased-array intracardiac echocardiography to guide transseptal catheterization during a catheter ablation procedure for atrial fibrillation (AF).

found that the LACA approach is superior. However, neither approach has become dominant. At many centers, a hybrid approach is used where wide-area circumferential ablation is performed around the left and right PV pairs guided by the electroanatomic mapping system. Additional lesions are delivered closer to the ostium to achieve electrical isolation guided by a circular mapping catheter.

Alternative ablation concepts include targeting fractionated complex atrial electrograms in the LA and right atrium, which may represent driving rotors that perpetuate AF, and ablating sites associated with a vagal response in an effort to modify the neural input to the atria (Figure 14.2).

14.6. Success Rates and Complications

The success rate for catheter ablation for AF depends on whether the AF is paroxysmal or persistent and the underlying substrate, and ranges between 50% and 95% in the literature. In experienced centers, the risk of a major complication associated with most LA ablation strategies, including PV stenosis,[7] cardiac tamponade, stroke, and death, is ~2–3%. A fistula between the LA and esophagus has been described as a rare complication of posterior LA ablation and has been associated with death. This complication has led most interventional electrophysiologists to avoid the use of large-tip electrodes or to reduce the power and temperature settings when delivering RF current.

Many steps are taken to reduce the risk of thromboembolism associated with the LA ablation. A transesophageal echocardiogram is performed in patients who are in persistent AF preoperatively. High doses of heparin are administered during the procedure usually to maintain an activated clotting time above 350 s, heparin is restarted after vascular sheaths are removed, and patients are discharged the following day with injections of low molecular weight heparin until the warfarin is therapeutic. Warfarin is continued for at least 2 months.

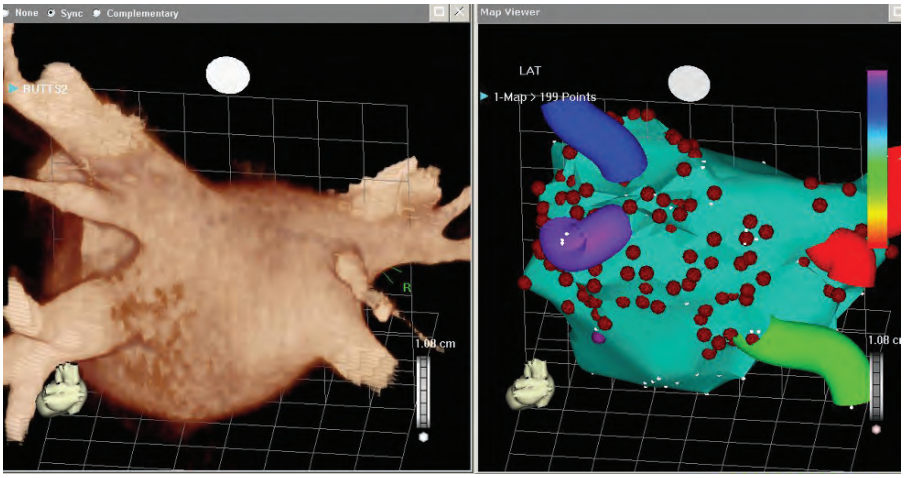


FIGURE 14.2. Example of a three-dimensional CT image of the left atrium and pulmonary veins displayed next to an electroanatomic map of the same patient during a catheter ablation procedure for atrial fibrillation (AF).

Key Points to Remember

- Catheter ablation of atrial fibrillation has been developed to a great degree of sophistication.
- At present, these endocardial lesions are typically created with the aid of unipolar radiofrequency ablation, guided by intra-cardiac echocardiography.

References

1. Knight BP, Weiss R, Bahu M, et al. A cost comparison of radiofrequency modification and ablation of the atrioventricular junction in patients with chronic atrial fibrillation. Circulation. 1997;96:1532-1536.
2. Haines DE, Hummel JD, Knight BP, Moulton KP, and MECA Investigators. Linear atrial ablation with the multiple electrode catheter ablation (MECA) system for atrial fibrillation: Final report. Pacing Clin Electrophysiol. 2002;25:637.
3. Haissaguerre M, Shah DC, Jais P, et al. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med. 1998;339:659-666.
4. Haissaguerre M, Shah DC, Jais P, et al. Electrophysiology breakthroughs from the left atrium to the pulmonary veins. Circulation 2000;101:2463-2465.
5. Hsu L-F, Jaïs P, Sanders P, et al. Catheter ablation for atrial fibrillation in congestive heart failure. N Engl J Med. 2004;351:2373-2383.
6. Pappone C, Rosanio S, Oreto G, et al. Circumferential radiofrequency ablation of pulmonary vein ostia. Circulation. 2000;102:2463-2465.
7. Saad EB, Marroche NF, Saad MD, et al. Pulmonary vein stenosis after catheter ablation of atrial fibrillation: Emergence of a new clinical syndrome. Ann Intern Med. 2003;138:634-638.

DropBooks

15
Surgical Therapy for Atrial Fibrillation

G. Bolotin and J.G. Maessen

15.1. Background

The first modern successful surgical approach to atrial fibrillation (AF) was presented in 1980 by Boineau, Cox, and coworkers.[1] They described left atrial isolation, which was capable of confining AF to the left atrium while leaving the remainder of the heart in normal sinus rhythm. However, since the left atrium continued to fibrillate, the risk of thromboembolism remained unchanged. The corridor procedure, described by Guiraudon in 1985, isolated a band of atrial septum, including the SA node and the AV node.[2] Again, the disadvantage was that both atria continued to fibrillate postoperatively. The results were therefore disappointing, in terms of both the hemodynamics and the risk for thromboembolism. After talented and thorough basic research on animal models, Cox and coworkers presented the Maze procedure aimed at directing the propagation of the sinus impulse throughout both atria, thereby restoring normal cardiac hemodynamics and reducing the risk for thromboembolism.[3]

15.2. The Maze Procedure

The Maze I procedure was presented in 1991.[4] However, because of some late chronotropic complications and intra-atrial conduction delays that resulted in decreased left atrial contraction, a modification named Maze II was presented.[5] A third version of the procedure (Maze III) was presented in 1995 in order to simplify the procedure.[6] In the Cox-Maze III operation, incisions and cryolesions are strategically made to interrupt the multiple reentrant circuits of AF. Right and left atrial incisions interrupt the most common reentrant circuits and direct the sinus impulse from the sinoatrial node to the atrioventricular node along a specified route.

15.2.1. Maze III Surgical Technique

The right atrial appendix is excised, leaving at least 2 cm of visible atrial tissue between the incision and the anterior superior vena cava (SVC). A second perpendicular incision is made from the middle of the first incision 2 cm down toward the free wall of the right atrium. A posterior longitudinal right atriotomy is then placed from the SVC toward the inferior vena cava (IVC). From the latter incision, another perpendicular incision is made 1 cm above the IVC cannula, and up to the tricuspid annulus. An adjuvant cryolesion is added at the level of the annulus to be certain that no fibers capable of conduction will be left. The last incision on the right side is directed anterolaterally from the excised appendix, and up to the tricuspid annulus. This is accompanied by an adjuvant cryoablation at the annular level. The left atrial and septal incisions include a standard left atrial incision in the interatrial groove and another incision of the atrial septum through the fossa ovalis. The first incision in the interatrial groove is then enlarged under vision to encircle and isolate the pulmonary veins from the left atrium. The last part of the circle is completed with cryoablation. The left atrial appendix is amputated from the inside. The last incision is from the pulmonary circle

toward the mitral annulus. To complete that part of the procedure, cryoablation is performed at the mitral annulus level and around the coronary sinus. All incisions made are closed using a continuous suturing technique. In 2000, Cox presented a minimally invasive modification for the procedure in which cryolesions replace most of the incisions and the left atrial appendage (LAA) does not need to be removed. The orifice of the appendage was cryoablated circumferentially and then closed from inside the left atrium.[7]

15.2.2. Maze III Results

The Cox-Maze III operation is the gold standard for surgical treatment of AF. Cox and colleagues have reported excellent results of patients undergoing Cox-Maze procedures of all types.[8] Out of 346 patients, operative mortality was 2%. AF was cured in 99%, and only 2% required long-term postoperative antiarrhythmic medication. Successful ablation of AF was unaffected by the presence of mitral valve disease, left atrial size, and type of AF (paroxysmal vs persistent). Temporary postoperative AF was common, occurring in 37% of patients. The authors' explanation was that because of the immediate postoperative period and until the atria heal from surgery, local refractory periods may be much shorter and thus the macro-reentrant circuits can be much smaller.[9] Fifteen percent of patients required new pacemakers after surgery. Right atrial transport function was demonstrated in 98% and left atrial transport function in 93%.

The results of the Maze III as reported by other centers were less favorable. At the Cleveland Clinic and Mayo Clinic, late freedom from AF is reported to be around 90%.[10] In a wide review of all the published data done by Khargi and coworkers in 2005, the results of 1,553 patients who underwent Maze III (out of 16 publications) are summarized.[11] The mean postoperative SR rates were 84.9%. Personal experiences of the editor of this book and Dr Melo from Carnaxide, Portugal, with the cut-and-sew maze procedure have been even less favorable. Major limitations of many of the follow-up studies of these surgical series are that they often relied on postal or telephonic follow-up. Atrial transport function was frequently measured with erroneous measures such as transmitral Doppler velocities (such as E/A ratios). Despite the supposed excellent results of the Maze procedure from the early 1990s onwards, less than 4,000 cut-and-sew maze procedures have been performed worldwide. This may also be in part due to longer operative times and increased morbidity and mortality of this procedure.

15.3. Less-Invasive Surgical Procedures

15.3.1. Partial Mazes

Many groups have reported procedures[12,13] that include some of the incisions and cryoablation lesions of the Cox-Maze III operation, but not all; these are categorized as partial-Maze procedures. They tend to focus on the left atrium, including isolation of the pulmonary veins and excision or exclusion of the left atrial appendage. They generally ignore the coronary sinus, which supposedly increases the risk of atrial flutter.[14]

15.3.2. Alternative Energy Sources to the Classical Cut-and-Sew Technique

In the last few years, several alternative energy sources have been introduced for ablating the heart tissue during AF surgical procedures.[14] The main advantages are less time and less risk as compared to the classic Maze III. The main problem with all of the energy sources is whether or not a transmural lesion is achieved (Figure 15.1).

15.3.3. Radiofrequency

Unipolar, unipolar with irrigated cooling, and bipolar systems with irrigated cooling are available in the market. The unipolar probes are used mainly endocardially, though there have been reports of unipolar epicardial applications also. Bipolar radiofrequency ablation is usually for epicardial ablation. Most bipolar systems have a flaw in that high impedance is often equated with a transmural lesion. Probably, the bipolar systems have some advantage in creating transmural lesions because of capture of the tissue between the electrodes. However, bunching of the tissue and incomplete coverage may be an issue. Furthermore, connecting lesions to remote areas of the left and right atrium is impossible to achieve. Although lesions sets

DropBooks

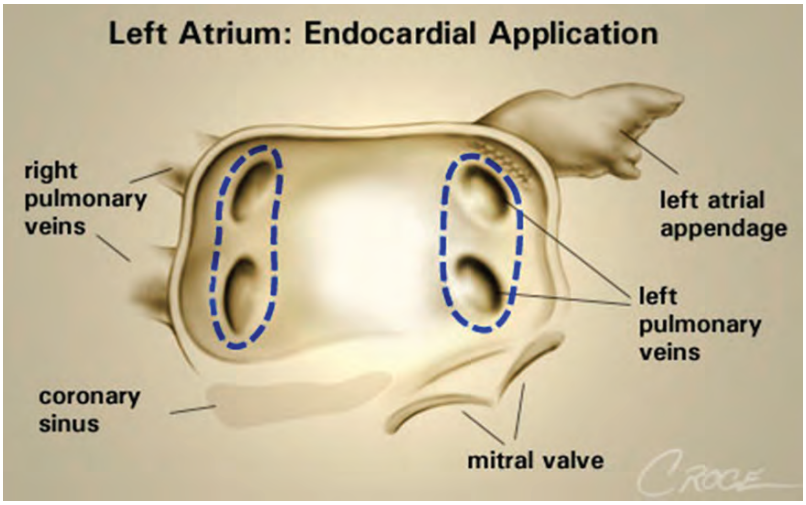


FIGURE 15.1. Early endocardial lesion set—proposed by Melo, based on bilateral isolation of pulmonary veins with left atrial appendage (LAA) closure.



FIGURE 15.2. Cobra-adhere—unipolar radiofrequency ablation device.



FIGURE 15.3. Medtronic Cardioblate, a bipolar irrigated radiofrequency ablation device that has been used widely in Europe.

created with radiofrequency energy vary, results are similar: AF is ablated in 70–80% of patients.[15–17] Perioperative AF after radiofrequency ablation is common, occurring in approximately two-thirds of patients[18] (Figure 15.2).

This device delivers unipolar radiofrequency to the atrial along with some weak suction to promote contact of the electrodes with the tissue (Figures 15.3 and 15.4).

15.3.4. Microwave

The microwave probes are used mainly epicardially. The long Flex 10 probe was designed to be used for minimally invasive approaches and robotic-assisted ablation.[19,20]

15.3.5. Cryoablation

Sueda and colleagues reported successful ablation using cryothermy ablation.[21] Gaita and coworkers have reported limited left atrial cryoablation combined with isolation of the pulmonary veins cures AF in ~70% of patients[22] (Figures 15.5 and 15.6).

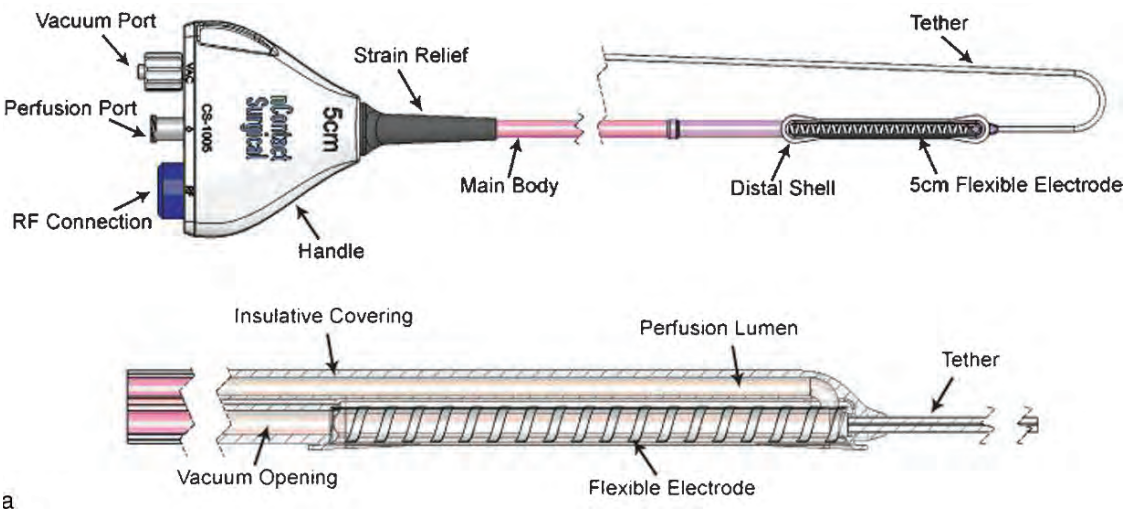




FIGURE 15.4. (a) Schematic representation of the n contact probe (b) The n contact radio-frequency fluid cooled probe.

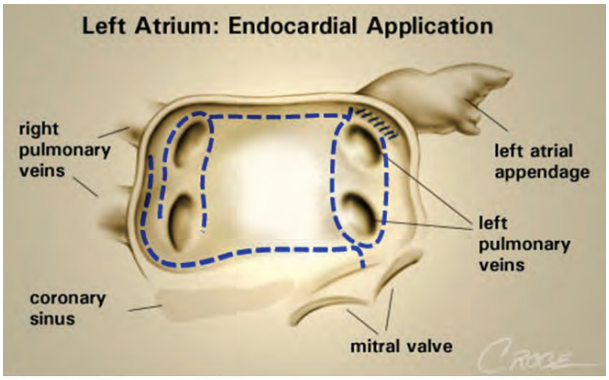
DropBooks



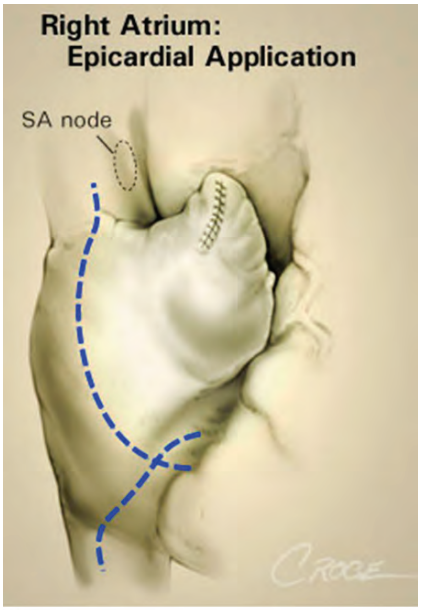
FIGURE 15.5. Surgifrost–Cryoprobe which incorporates the flexibility of the early Cobra radiofrequency (RF) probe and reliable cooling of the tissue to less than −100 °C

15.4. The Issue of Transmurality in Surgical Ablation for Atrial Fibrillation

The only goal of producing lesions with any ablation tool is the substitution of conducting tissue by nonconducting, scar tissue. The golden standard has been supposedly set by the "cut-and-sew" technique in the original Cox-Maze procedure. This is a "gold standard" that few discerning surgeons and even fewer in the cardiological community accept. In percutaneous ablation approaches, cardiologists have translated this goal in achieving conduction block as evidenced by electrophysiological measurements. The percutaneous approach allows checking for conduction block during the intervention. In line with the Maze procedure, surgeons redefined this goal into the production of histologically transmural lesions. In contrast to their cardiology colleagues, they can check the histological quality of their lesions only by indirect means. Despite excellent clinical results obtained by surgeons in treating AF, recent studies have shown that the establishment of histologically transmural lesions is not as obvious as generally assumed. The question is whether this is important for our routine ablation procedures, and if so, how should we deal with it, based on the current evidence available.[23–26]



a



b

FIGURE 15.6. The proposed lesion sets on the right (**a**) and the left atria (**b**) that have the best likelihood of replicating the Cox-Maze III lines of block with a variety of energy sources.

Tissue characteristics considerably influence the continuity of lesions and lesion depth in the first place. The thickness of the atrial wall may vary tenfold within one ablation line. Similarly, the amount of fat tissue present in the different areas around the pulmonary veins shows a high intra and interindividual variability. Furthermore, trabeculated areas creating bridges from isolated regions to normal conducting tissue may be responsible for persistent conduction. In the elderly and in patients with manifest hypertrophy of the atrial tissue, the presence of scattered fibrosis may offer another hurdle for ablation techniques to make smooth, consistent lesions. The temperature of the tissue and its surroundings is also likely to affect the lesion depth but poorly studied in the clinical setting. Beating heart versus the arrested heart, hypothermic perfusion versus normothermic perfusion, epicardial versus endocardial, all these approaches offer different environmental conditions for the ablation tools. An experimental study suggested that with radiofrequency ablation the endocardial approach is more effective than the epicardial approach. It is very likely that these unpredictable and mostly uncontrollable conditions determine the quality of a lesion set rather than the energy source used for the ablation or the design of the tool.[23,24,27]

Most information on the quality of ablation lesions has been offered by studies on isolating pulmonary veins. The human anatomy allows ablation of the pulmonary veins, one by one, two by two, and sometimes, all four or five together in one encircling. The existence of an entrance and exit block between the pulmonary vein area and the atrial tissue, proving electrophysiological isolation, can thus be easily determined by monitoring the EKG during pacing from within and outside the isolated area. From such studies, the need for transmurality and the equivalence between transmurality and electrophysiological isolation has been questioned. First, it was shown that transmurality may not be obtained until several weeks after ablation whereas electrical isolation is achieved immediately during the procedure, suggesting that lesions may develop in time. Second, an autopsy study revealed that certain patients in sinus rhythm with proven conduction block during surgery

appear to have incomplete continuity of their lesion set and partially, incomplete transmural lesions at autopsy.[27] This observation was confirmed in a study in which 58 ablation lesions from seven patients who died between 2 and 22 days postoperatively were studied.[28] These seven patients had a concomitant antiarrhythmic procedure using saline irrigated cooled tip radiofrequency ablation (SICTRA) to treat permanent AF. Histological examination showed transmurality in 96–100% of the SICTRA lesions at the pulmonary vein orifices and the posterior left atrial wall, but only in 14% of the left atrial isthmus lesions, resulting in an overall transmurality rate of 76% of the induced SICTRA lesions. Finally, it was recently demonstrated that in a large group of patients with clinically successful treatment and proven electrophysiological block initially during the intervention, conduction block was lost several months after the ablation procedure without recurrence of AF.[29] What all these means clinically is open to question. The left atrial isthmus lesion, along with the coronary sinus lesion, was insisted as being essential by Cox, based on anecdotal experience with a few patients and this may in itself be fallacious.

From these observations, one can only conclude that our current understanding of the success of our ablation procedures is at least incomplete. In an effort to address this problem, a recent experimental study showed that the effect of isolating the pulmonary veins is not an all-or-non phenomenon. Complete isolation of the pulmonary veins revealed a 100% success rate. However, if deliberately a gap was left in the encircling of the veins, still a very significant reduction in the susceptibility of the atrial tissue for AF was observed.[20] However, these were animal studies not conducted in a chronic AF model. These findings may offer an explanation for the discrepancy between the claims and reality of relatively high success rate of today's pulmonary veins ablation procedures despite the conflicting data about continuity and transmurality of the lesions produced by these techniques. Apparently, these procedures not only affect the pulmonary veins but other structures involved in the initiation or maintenance of AF as well.[30–34]

Transmurality has become an important issue, partly because several companies claim that their tools create transmural lesions, suggesting that others do not. Comparative, clinical studies are in progress but do not yet allow final conclusions on superior efficacy of certain tools. The current clinical impact of the transmurality issue is difficult to assess. A recently published systematic review offered some important hints in this respect. The results of the classic "cut-and-sew" Cox-Maze III procedures were compared to results of procedures using alternative sources of energy to obtain a biatrial lesion patron. Patients in the first group had a 85.3% postoperative SR conversion rate versus 79.7% in the ablation group. If this difference of 5.6% can be completely attributed to problems in achieving transmurality, the impact is distinct but small.[11] This may also be partly due to inadequate appreciation of the limitations of each of the alternative energy sources by the surgeons.

On the basis of the currently available evidence, one might conclude that histological transmurality is not a prerequisite for clinical success. Measuring the occurrence of a conduction block during ablation is an informative but not conclusive tool to determine successful treatment. Sophisticated mapping techniques might appear necessary to guide ablation strategies and control its efficacy in the future. More comparative clinical as well as experimental studies are needed to test the effectiveness of various ablation tools in this respect. The ultimate target for more successful ablation procedures has yet to be defined.

DropBooks

15.5. Results

In general, the results of all ablation-based surgical procedures range around 70% sinus rhythm at 6 months postoperatively. Neither energy source nor surgical technique (excluding the classic Maze III procedure) has been found to be superior. The reason for this is probably multifactorial, including lack of transmural lesions in many cases, different lines of ablation, and different patient selection as compared to that in Cox's reports.[11,14] As mentioned before, this may be partly because of misleading advertising by the various vendors: surgeons using the techniques are not as familiar with the limitations of their energy sources as cutting-and-sewing. Another reason for the lack of a clear difference between the various procedures was suggested by Thomas and coworkers, who reported that pulmonary vein isolation is indeed an advan-

tage; however, a block of AF was demonstrated in significant cases without completely successful pulmonary vein isolation.[20]

The results of the less-invasive approach for surgical treatment of AF are good enough to perform ablation for both paroxysmal and chronic AF in most of the patients undergoing cardiac operations for other indications. However, it is clear that more preclinical and clinical work should be done before surgical treatment will be indicated on a wide scale for patients with isolated AF.

15.5.1. Keypoints to Remember

Surgical ablation for AF is a growing area of development and use. While the Cox-Maze cut-and-sew experience is considered the "gold standard," it must be realized that those experiments that formed the foundations of this arena were performed in animals with an acute model of AF. The best therapy may yet be guided by detailed mapping of the atria. Surgically, the most important aspect seems to be obliteration of atrial appendages to reduce the thrombo-embolic risk.

References

1. Williams JM, Ungerleider RM, Lofland GK, Cox JL. Left atrial isolation: New technique for the treatment of supraventricular arrhythmias. *J Thorac Cardiovasc Surg*. 1980;80:373.
2. Guiraudon GM, Campbell CS, Jones DL, et al. Combined sino-atrial node atrio-ventricular node isolation: A surgical alternative to His bundle ablation in patients with atrial fibrillation. *Circulation*. 1985;72(suppl 3):220.
3. Cox JL, Schuessler RB, D'Agostino HJ Jr, et al. The surgical treatment of atrial fibrillation, III: Development of a definite surgical procedure. *J Thorac Cardiovasc Surg*. 1991;101:569.
4. Cox JL. The surgical treatment of atrial fibrillation, IV: Surgical technique. *J Thorac Cardiovasc Surg*. 1991;101:584.
5. Cox JL, Boineau JP, Schuessler RB, Lappas DG. Modification of the Maze procedure for atrial flutter and atrial fibrillation, I: Rationale and surgical results. *J Thorac Cardiovasc Surg*. 1995;110:473.
6. Cox JL, Jaquiss RD, Schuessler RB, Boineau JP. Modification of the Maze procedure for atrial flutter and atrial fibrillation, II: Surgical technique of the Maze III procedure. *J Thorac Cardiovasc Surg*. 1995;110:485.
7. Cox JL. The minimally invasive Maze-III procedure. *Oper Tech Thorac Cardiovasc Surg*. 2000;5:79.
8. Cox JL, Ad N. The importance of cryoablation of the coronary sinus during the Maze procedure. *Semin Thorac Cardiovasc Surg*. 2000;12:20-24.
9. Cox JL. Surgical treatment of supraventricular tachyarrhythmias. In: Cohn LH, Edmunds LH Jr, eds. *Cardiac Surgery in the Adult*. New York: McGraw-Hill; 2003:chap 53.
10. McCarthy PM, Gillinov AM, Castle L, Chung M, Cosgrove D, 3rd. The Cox-Maze procedure: The Cleveland Clinic experience. *Semin Thorac Cardiovasc Surg*. 2000;12:25-29.
11. Khargi K, Hutten BA, Lemke B, Deneke T. Surgical treatment of atrial fibrillation; a systematic review. *Eur J Cardiothorac Surg*. 2005;27:258-265.
12. Sueda T, Nagata H, Shikata H, et al. Simple left atrial procedure for chronic atrial fibrillation associated with mitral valve disease. *Ann Thorac Surg*. 1996;62:1796-1800.
13. Takami Y, Yasuura K, Takagi Y, et al. Partial maze procedure is effective treatment for chronic atrial fibrillation associated with valve disease. *J Card Surg*. 1999;14:103-108.
14. Gillinov AM, Blackstone EH, McCarthy PM. Atrial fibrillation: Current surgical options and their assessment. *Ann Thorac Surg*. 2002;74:2210-2217.
15. Williams MR, Stewart JR, Bolling SF, et al. Surgical treatment of atrial fibrillation using radiofrequency energy. *Ann Thorac Surg*. 2001;71:1939-1944.
16. Abreu Filho CA, Lisboa LA, Dallan LA, et al. Effectiveness of the maze procedure using cooled-tip radiofrequency ablation in patients with permanent atrial fibrillation and rheumatic mitral valve disease. *Circulation*. 2005;112(9, suppl):I20–I25.
17. Miyairi T, Nakao M, Kigawa I, et al. A closed biatrial procedure using bipolar radiofrequency ablation. *J Thorac Cardiovasc Surg*. 2006;132(1):168-169.
18. Benussi S, Pappone C, Nascimbene S, et al. A simple way to treat chronic atrial fibrillation during mitral valve surgery: the epicardial radiofrequency approach. *Eur J Cardiothorac Surg*. 2000;17:524-529.
19. Reade CC, Johnson JO, Bolotin G, et al. Combining robotic mitral valve repair and microwave atrial fibrillation ablation: Techniques and initial results. *Ann Thorac Surg*. 2005;79(2):480-484.
20. van Brakel TJ, Bolotin G, Nifong LW, et al. Robot-assisted epicardial ablation of the pulmonary veins: Is a completed isolation necessary? *Eur Heart J*. 2005;26(13):1321-1326. Epub 2005 Jan 6.
21. Sueda T, Nagata H, Shikata H, et al. Simple left atrial procedure for chronic atrial fibrillation associated

with mitral valve disease. *Ann Thorac Surg*. 1996;62: 1796-1800.
22. Gaita F, Gallotti R, Calo L, et al. Limited posterior left atrial cryoablation in patients with chronic atrial fibrillation undergoing valvular heart surgery. *J Am Coll Cardiol*. 2000;36:159-166.
23. Melo J, Adragao P, Neves J, et al. Endocardial and epicardial radiofrequency ablation in the treatment of atrial fibrillation with a new intra-operative device. *Eur J Cardiothorac Surg*. 2000;18:182-186.
24. Thomas SP, Guy DJR, Boyd AC, Eipper VE, Ross DL, Chard RB. Comparison of epicardial and endocardial linear ablation using handheld probes. *Ann Thorac Surg*. 2003;75:54-548.
25. Santiago T, Melo J, Gouveia RH, et al. Epicardial radiofrequency applications: In vitro and in vivo studies on human atrial myocardium. *Eur J Cardiothorac Surg*. 2003;24:481-486.
26. van Brakel TJ, Bolotin G, Salleng K, et al. Evaluation of epicardial microwave ablation lesions: Histology versus electrophysiology. *Ann Thorac Surg*. 2004;78:1397-1402.
27. Accord RE, van Suylen RJ, van Brakel TJ, Maessen JG. Post-mortem histological evaluation of microwave lesions after epicardial pulmonary vein isolation for atrial fibrillation. *Ann Thorac Surg*. 2005. In press.
28. Deneke T, Khargi K, Muller KM, et al. Histopathology of intraoperatively induced linear radiofrequency ablation lesions in patients with chronic atrial fibrillation. *Eur Heart J*. 2005;[Epub ahead of print] (doi: 20.1093/eurheartj/ehi255).
29. Kottkamp H, et al. Time courses and quantitative analysis of atrial fibrillation episode number and duration after circular plus linear left atrial lesions: Trigger elimination or substrate modification: early or delayed cure? *J Am Coll Cardiol*. 2004;44:869-877.
30. Betts TR, Roberts PR, Morgan JM. Feasibility of a left atrial electrical disconnection procedure for atrial fibrillation using transcatheter radiofrequency ablation. *J Cardiovasc Electrophysiol*. 2001;12: 1278-1283.
31. Hwang C, Wu TJ, Doshi RN, Peter CT, Chen PS. Vein of Marshall cannulation for the analysis of electrical activity in patients with focal atrial fibrillation. *Circulation*. 2000;101:1503-1505.
32. Wu TJ, Ong JJ, Chang CM, et al. Pulmonary veins and ligament of Marshall as sources of rapid activations in a canine model of sustained atrial fibrillation. *Circulation*. 2001;103:1157-1163.
33. Schauerte P, Scherlag BJ, Pitha J, et al. Catheter ablation of cardiac autonomic nerves for prevention of vagal atrial fibrillation. *Circulation*. 2000;102: 2774-2780.
34. Chiou CW, Eble JN, Zipes DP. Efferent vagal innervation of the canine atria and sinus and atrioventricular nodes. The third fat pad. *Circulation*. 1997;95:2573-2584.

DropBooks

16
Pacing Therapies, Defibrillators, and Post-Operative Arrhythmias

Bradley P. Knight

16.1. Introduction

Ventricular dysfunction is associated with myocardial fibrosis, dilatation, and hypertrophy. The syndrome of congestive heart failure (CHF) caused by ventricular dysfunction leads to sympathetic activation and abnormal electrophysiology. These factors predispose patients with CHF to atrial and ventricular tachyarrhythmias by providing the substrate for reentry and by causing the triggers that lead to arrhythmias caused by triggered activity and abnormal automaticity. Patients with CHF also commonly have conduction disease that is manifest as sinus node dysfunction, atrioventricular block, and intraventricular conduction delays.

Once a patient with CHF develops atrial fibrillation (AF), heart failure symptoms worsen and a negative feedback loop is established. The presence of AF is an independent predictor of an increase in mortality in many heart failure trials. Aggressive therapy directed at each problem is necessary in patients with CHF and AF. Patients with CHF are at an increased risk of sudden cardiac death caused by ventricular tachycardia (VT) and fibrillation. These patients should be considered for implantable devices therapy for the prevention of sudden death.

This chapter will discuss implantable cardiac rhythm management device therapy for patients with CHF. Because arrhythmias such as AF and heart block are common following cardiac surgery, therapy for these arrhythmias will also be covered.

16.2. Prevention of Sudden Death in Patients with Heart Failure

Left ventricular dysfunction is a well-established risk factor for sudden death. The clinical syndrome of congestive heart failure (CHF) itself can also contribute to arrhythmogenesis in patients with ventricular dysfunction and can increase mortality in patients with either an ischemic or nonischemic dilated cardiomyopathy, independent of ejection fraction. Unfortunately, antiarrhythmic drugs have not been found to improve mortality in patients with CHF. In fact, the use of sodium channel blockers such as flecainide increases mortality in patients post myocardial infarction.

Defibrillator therapy has been shown to improve mortality among patients with CHF and left ventricular dysfunction. The Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) found a mortality benefit from defibrillator therapy for primary prevention among patients with CHF and either an ischemic or nonischemic dilated cardiomyopathy.[1,2] This trial prompted a revision of the coverage guidelines for implantable defibrillator by the Center for Medicare & Medicaid Services (CMS) in 2005.[3] This coverage decision provides a reasonable guideline when evaluating patients for defibrillator therapy. Patients who should be considered for implantable defibrillator for primary prevention include the following:

1. Patients with ischemic dilated cardiomyopathy, documented prior myocardial infarction, New York Heart Association (NYHA) class II and III

heart failure, and measured left ventricular ejection fraction (LVEF) of ≤35%;
2. Patients with nonischemic dilated cardiomyopathy of >9 months, NYHA class II and III heart failure, and measured LVEF of ≤35%;
3. Patients who meet all current CMS coverage requirements for a cardiac resynchronization therapy (CRT) device and have NYHA class IV heart failure.

Patients must not have the following characteristics:

1. Cardiogenic shock or symptomatic hypotension while in a stable baseline rhythm;
2. Had a coronary artery bypass graft (CABG) or percutaneous transluminal coronary angioplasty (PTCA) within the last 3 months;
3. Had an acute myocardial infarction within the last 40 days;
4. Clinical symptoms or findings that would make them a candidate for coronary revascularization;
5. Irreversible brain damage from preexisting cerebral disease;
6. Any disease, other than cardiac disease (e.g., cancer, uremia, liver failure), associated with a likelihood of survival less than 1 year (Figure 16.1).

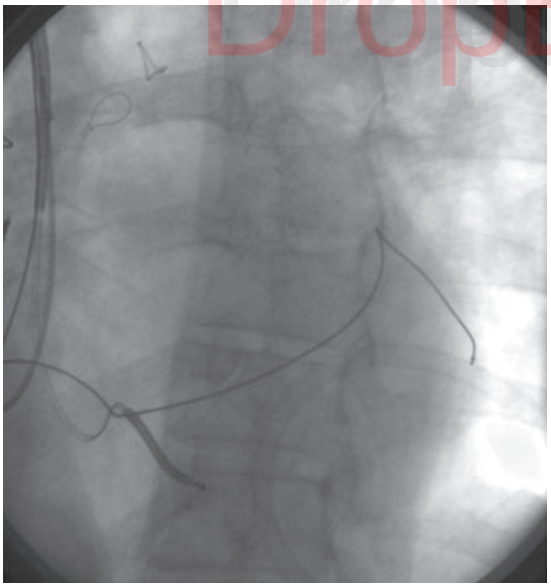


FIGURE 16.1. A fluoroscopic image of a transvenous defibrillator system that delivers cardiac resynchronization therapy by simultaneously pacing from the right ventricular defibrillator lead and the left ventricular coronary vein pacing lead.

16.3. Cardiac Resynchronization Pacing Therapy

16.3.1. Background

Intraventricular conduction disturbances are common in patients with CHF. Up to one-third of patients with heart failure have a bundle branch block and a QRS duration greater than 120 ms. An intraventricular conduction delay is a marker of more severe myocardial disease, but also causes a reduction in cardiac output and worsening heart failure by causing inter- and intraventricular dyssynchrony. In addition, a bundle branch block can worsen mitral regurgitation by changing the ventricular activation sequence. The severity of the intraventricular conduction delay has been shown to correlate directly with mortality in patients with heart failure.

The principle behind resynchronization pacing therapy is to simultaneously pace at two or more ventricular sites to minimize the time required for ventricular activation and improve cardiac synchrony. Several acute hemodynamic studies have shown that biventricular pacing improves inter- and intraventricular synchrony, mitral regurgitation, and diastolic function. Biventricular pacing has also been shown to improve cardiac efficiency by increasing cardiac work without increasing myocardial oxygen consumption.

16.3.2. Clinical Trials of Permanent Biventricular Pacing

Multiple clinical trials have been performed to measure the effect of permanent biventricular pacing in patients with advanced heart failure and ventricular dyssynchrony. The trials can be divided into two groups based on whether or not the patients had an indication for defibrillator therapy. These trials have demonstrated that CRT is associated with an improvement in functional capacity based on quality of life, exercise oxygen consumption, and heart failure classification. A meta-analysis of four major randomized trials revealed a significant 51% reduction in mortality from progressive heart failure in the 1,634 patients studied.[4]

The largest trial of CRT was the Comparison Of Medical Therapy, Pacing, and Defibrillation

DropBooks

in Heart Failure (COMPANION) trial. Patients were required to have a dilated cardiomyopathy, LVED dimension of >60 mm, NYHA functional classification III–IV symptoms, ejection fraction of <0.35, QRS duration of >120 ms, a PR interval of >150 ms, and at least one hospitalization for CHF in the previous 12 months. Patients were randomized to one of three arms: biventricular pacemaker, an implantable defibrillator with biventricular pacing, or no device, in a 2:2:1 ratio. The trial was stopped prematurely after 1,600 of the anticipated 2,200 patients were enrolled, due to a statistically significant 20% reduction in the primary endpoint of combined all-cause mortality and hospitalizations in the biventricular pacing arm (one-half biventricular pacemakers and one-half biventricular pacing defibrillators) as compared to no pacing. The absolute mortality rates after 1 year of follow-up were 19%, 15%, and 11% for the no pacing, biventricular pacing, and biventricular pacing defibrillator groups, respectively.

16.3.3. Current Indications for CRT

Patients with advanced, medically refractory CHF and ventricular dyssynchrony should be considered for CRT. Because the etiology of heart failure does not appear to be predictive of response to CRT, patients with or without coronary artery disease are candidates for biventricular pacing The current indications for CRT include NYHA class III or IV CHF symptoms, LVEF of <35%, and a QRS duration of >120 ms. The QRS duration is a convenient method to identify patients with ventricular dyssynchrony, but is an imprecise measure of mechanical dyssynchrony. Therefore, alternative methods such as tissue Doppler real-time three-dimensional echocardiography are being investigated as alternative methods to measure ventricular dyssynchrony and to identify patients who might benefit from CRT.[5]

Ventricular pacing itself leads to ventricular dyssynchrony, regardless of the baseline QRS duration. Patients with advanced heart failure who require ventricular pacing should also be considered for biventricular pacing as an alternative to right ventricular pacing. Although patients with a bradycardia indication for a pacemaker were not included in most biventricular pacing trials, a study of patients who had undergone prior atrioventricular (AV) node ablation and right ventricular pacemaker implantation demonstrated a significant improvement in heart failure symptoms after an upgrade to a biventricular pacemaker.

16.3.4. Considerations Regarding CRT Device Implantation

Biventricular pacing is usually achieved by simultaneously pacing the right ventricle and the left ventricle. In patients who are in sinus rhythm, a right atrial lead is placed for atrial sensing to allow ventricular stimulation to occur shortly after atrial systole. Patients who are in sinus rhythm are usually paced with an AV delay that is shorter than the PR interval to maintain constant biventricular capture. Successful resynchronization therapy depends on continuous biventricular capture. It is difficult to maintain ventricular capture in patients with atrial fibrillation (AF) unless the ventricular response is slow or there is complete heart block. However, in general, patients with AF and intact AV conduction are candidates for CRT when AV conduction can be depressed with medications or catheter ablation.

Because patients who are candidates for CRT usually have severe ventricular dysfunction and are at risk for ventricular arrhythmias, it is not clear which patients are candidates for a biventricular pacemaker without defibrillator capabilities. There are six steps during implantation of a transvenous, atriobiventricular pacing device: implantation of a standard right-sided pacing or defibrillation lead, cannulation of the coronary sinus with a guiding sheath, coronary sinus venography, placement of a pacing lead in the coronary vein for left ventricular pacing, removal of guiding sheath, and attachment of the leads to the pacing generator. When a suitable left ventricular pacing site cannot be obtained from the coronary veins, permanent epicardial lead placement should be considered. New pericardial approaches and robotics are under development to achieve minimally invasive epicardial pacing. Devices that have programmable timing offset between the right ventricle and the left ventricle are also being evaluated in clinical trials to determine whether or not this function can further improve ventricular synchrony.

16.4. Management of Arrhythmias After Cardiac Surgery

16.4.1. Atrial Fibrillation

Arrhythmias are common following cardiac surgery. AF is the most common sustained arrhythmia after heart surgery and occurs in about 20–40% of patients.[6] Although some studies have found that minimally invasive cardiac surgery and surgery without the use of cardiopulmonary bypass are associated with a lower incidence of postoperative arrhythmias, the incidence of AF remains high.

Postoperative AF usually occurs within 1 week of surgery and has a peak incidence on postoperative day 2. Although the arrhythmia usually resolves over time, postoperative AF is associated with significant morbidity, prolongation of length of stay, and increased costs. Multiple mechanisms contribute to postoperative AF; however, sympathetic stimulation and pericarditis are important factors. Age appears to be the most powerful, independent predictor of postoperative AF. Additional risk factors include valvular heart disease, chronic lung disease, atrial enlargement, and preoperative atrial arrhythmias.[7] Patients with risk factors for AF should be targeted with preventive strategies.

Most randomized, controlled trials of beta-blockers have demonstrated a protective effect for postoperative AF. However, many patients in these trials were on beta-blockers preoperatively. Therefore, the protective effect of beta-blockers that has been demonstrated may have been due partly to beta-blocker withdrawal in the placebo group. Nonetheless, beta-blockers appear to be protective for both AF and recurrent ischemic events in patients undergoing cardiac surgery and should be prescribed postoperatively unless there are contraindications.

Additional strategies have been found to further reduce the incidence of postoperative AF. For patients scheduled for elective cardiac surgery, 1 week of oral, preoperative amiodarone at a dose of 600 mg per day is highly effective and well tolerated for prevention of AF.[8] Postoperative intravenous (IV) amiodarone was found in the ARCH (Amiodarone Reduction in Coronary Heart) trial to significantly reduce the incidence of postoperative AF and is an option for patients who require urgent surgery. However, IV amiodarone is expensive and was not found to reduce hospital length of stay in the ARCH trial.[9]

Oral sotalol can prevent postoperative AF, but should be given in low doses to prevent ventricular proarrhythmia, and should be avoided in patients with renal insufficiency. Digoxin, verapamil, magnesium, and procainamide are not useful for prevention of postoperative AF.

Biatrial pacing appears to be a useful strategy to prevent postoperative AF.[10] The concept is that pacing more than one atrial site using temporary epicardial pacing wires causes less dispersion in atrial refractoriness and shortens the total atrial activation time compared to sinus rhythm or single-site atrial pacing.

The management of postoperative AF is similar to the management of AF that is not associated with surgery. Because a majority of AF resolves within a couple of months after surgery, rate control and anticoagulation is a reasonable alternative to restoration of sinus rhythm if the AF is well tolerated. In general, anticoagulation should be instituted for AF that persists for >48 h. However, the risk of anticoagulation in a patient who has just undergone cardiac surgery must be assessed on an individual basis. When the risk of anticoagulation with heparin is felt to be high in a patient who develops postoperative AF, prompt cardioversion within 48 h should be considered, so that anticoagulation can be avoided.

16.4.2. Ventricular Arrhythmias

Ventricular tachycardia and fibrillation can occur in patients with heart failure after cardiac surgery. Treatment should be based on standard Adult Cardiac Life Support guidelines. IV amiodarone is a useful drug to prevent recurrent arrhythmias while the patient is in the hospital. The use of antiarrhythmic drugs for asymptomatic nonsustained ventricular tachycardia should be avoided. Most patients do not require long-term therapy to prevent recurrent ventricular arrhythmias, because most of these arrhythmias are a result of reversible causes. However, when a reversible cause cannot be identified, patients should be considered for implantable defibrillator

DropBooks

therapy. Patients who have persistent ventricular dysfunction several weeks following heart surgery should be evaluated for defibrillator therapy as well regardless of a prior history of arrhythmias.

16.4.3. Bradycardia

Sinus node dysfunction and atrioventricular block (AVB) are not uncommon after heart surgery but are usually transient. AVB is more common after vavlular heart surgery compared to coronary bypass surgery and can be permanent. Patients can usually be treated acutely with dual-chamber pacing using the epicardial temporary pacing wires placed at the time of surgery. However, it is not always easy to determine whether to implant a permanent pacemaker early postoperatively or to continue to wait for return of conduction. Prior reports have recommended 3–21 days after the onset of high-degree AVB as a reasonable waiting period before pacemaker implantation. A recent study found that 11% of patients had complete AVB and 6% required permanent pacing after aortic and mitral valve surgery. The study suggested that if complete AVB is present within the first 24 h postoperatively and persists for > 48 h, it is unlikely to resolve within the next 1–2 weeks. The authors recommended that in patients otherwise ready for discharge, pacemaker implantation should be performed before postoperative day 7.[11]

References

1. Whang W, Mittleman MA, Rich DQ, et al. Heart failure and the risk of shocks in patients with implantable cardioverter defibrillators: Results from the Triggers of Ventricular Arrhythmias Study. *Circulation*. 2004;109:1386-1391.
2. Bardy GH, Lee KL, Mark DB, et al. The Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) Investigators. Amiodarone or an Implantable Cardioverter-Defibrillator for Congestive Heart Failure. *N Engl J Med*. 2005;352:225-237.
3. Moss A, Zareba W, Hall W, et al. Prophylactic implantation of a defibrillator in patients with myocardial infarction and reduced ejection fraction. For the Multicenter Automatic Defibrillator Implantation Trial II Investigators. *N Engl J Med*. 2002;346: 877-883.
4. Casey C, Knight BP. Cardiac resynchronization pacing therapy. *Cardiology*. 2004;101(1–3):72-78.
5. Leon A, Greenberg J, Kanuru N, et al. Cardiac resynchronization in patients with congestive heart failure and chronic AF effect of upgrading to biventricular pacing after chronic right ventricular pacing. *J Am Coll Cardiol*. 2002;39:1258-1263.
6. Ommen SR, Odell JA, Stanton MS. Atrial arrhythmias after cardiothoracic surgery [review]. *N Engl J Med*. 1997;336:1429-1434.
7. Falk RH. Etiology and complications of atrial fibrillation: Insights from pathology studies. *Am J Cardiol*. 1998;82:10N-7N.
8. Daoud EG, Strickberger SA, Man KC, et al. Preoperative amiodarone as prophylaxis against atrial fibrillation after heart surgery. *N Engl J Med*. 1997;337:1785-1791.
9. Guarnieri T, Nolan S, Gottlieb SO, Dudek A, Lowry DR. Intravenous amiodarone for the prevention of atrial fibrillation after open heart surgery: The Amiodarone Reduction in Coronary Heart (ARCH) trial. *J Am Coll Cardiol*. 1999;34:343-347.
10. Daoud EG, Dabir R, Archambeau M, Morady F, Strickberger SA. Randomized, double-blind trial of simultaneous right and left atrial epicardial pacing for prevention of post-open heart surgery atrial fibrillation. *Circulation*. 2000;102:761-765.
11. Kim MH, Deeb GM, Eagle KA, et al. Complete atrioventricular block after valvular heart surgery and the timing of pacemaker implantation. *Am J Cardiol*. 2001;87:649-651.

17
Ventricular Containment, Shape Change, and Infarct Restraint

Jai Raman

This chapter describes the concepts behind the shaping of the ventricle to prevent heart failure progression. The techniques described range from ventricular containment, infarct restraint, and stabilization to modifying the ventricle to reduce wall stress.

The left ventricle is a cone in three dimensions with an elaborated rugose and trabeculated endocardial surface. The right ventricle on the other hand is crescent shaped in cross-section and wraps around the right side of the left ventricle. In systolic heart failure, as the ventricles dilate, the normal shape and size of the ventricles get distorted. This then affects the Frank-Starling mechanism of the heart,[1] which was described initially by Frank in 1895 and further elaborated in 1914 by Patterson and Starling.[2] This describes the pressure–volume relationship of the left ventricle and the importance of preload in driving the mechanical properties of the heart as a pump. Unfortunately, most studies on cardiac physiology have been with them in the isolated heart preparation and are limited as being in one or two dimensions.

The left ventricle is best described in physical terms as a prolate spheroid and the equatorial region can be approximated as a thick-walled cylinder. Guccione et al. focused on this equatorial region to yield an analytically tractable boundary value[3] and the application of various laws, such as LaPlace's law.

Freeman collected pressure–volume data on intact pericardia from dogs and showed that pericardium acted as an effective constraint to deformations of the ventricles.[4] This served as the concept behind cardiomyoplasty and passive ventricular constraint.

The concept of shape change to alter wall stress in larger hearts is based on the application of LaPlace's law to the left ventricle. There are limitations to simple interpretation of this law and this may be the reason behind suboptimal results with the devices that advocate shape change as a means of controlling heart failure.

DropBooks

17.1. Ventricular Containment

Ventricular containment, constraint, or restraint is a concept that arose out of the experience with dynamic cardiomyoplasty. The positive outcomes with this procedure in the 1980s were shown to be due to constraint provided by the muscle wrap of the ventricles (constraint provided by cardiomyoplasty).We then proposed, based on suggestions by prominent surgeons including Stuart Jamieson, that we might dispense with the muscle and attempt passive constraint with a prosthetic mesh. Our early proof of concept experiments performed at the Austin Hospital, Melbourne, in 1997 showed that passive ventricular constraint prevented progression of heart failure.[5]

Drs John Power and Raman then proceeded to study a large group of sheep in various stages of heart failure to establish the role of passive ventricular constraint in halting the progression of heart failure.[6] Based on our animal work and similar experiments with another model of heart failure at Detroit,[7] the concept of ventricular con-

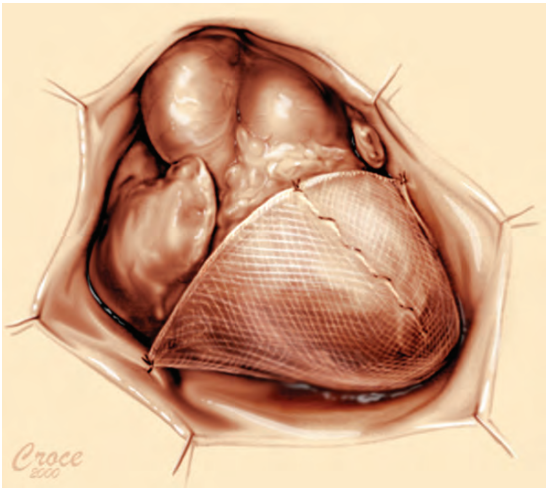


FIGURE 17.1. Ventricular containment as a concept. Schematic diagram of a heart contained by polyester mesh.

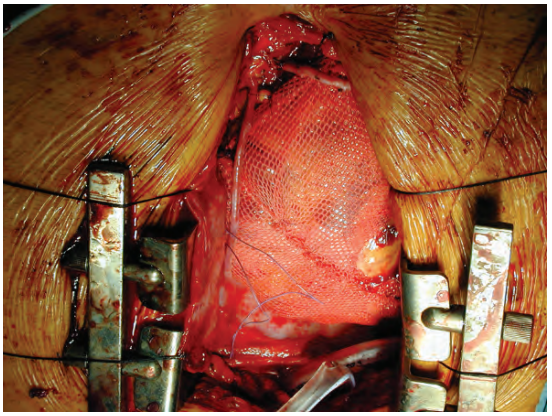


FIGURE 17.2. Operative photograph of one of the first implants of the Acorn cardiac support device. Operative photograph of a contained ventricle in the setting of CABG (1999). Note the window in the mesh cut away for a distal anastomosis of a graft.

straint was studied in human patients by a start-up company called Acorn Cardiovascular, Inc. The first human procedure was performed at the Austin Hospital in Melbourne on April 19, 1999, by Raman and colleagues. Thereafter, a phase 1 study was performed in Berlin and Melbourne. Figure 17.1 shows an artist's depiction of the mesh containing the heart. Based on this early experience, a pivotal trial was conducted in the USA with 15 participating centers. The results of this study were presented at the 2004 annual scientific sessions of the American Heart Association (AHA). Figure 17.2 shows the operative photograph of one of the first patients who underwent this procedure at the Austin Hospital, Melbourne.

17.1.1. Summary of Randomized Study of the Acorn Cardiac Support Device

300 Patients with Heart Failure

81.3% New York Heart Association (NYHA) class III, 3.7% class IV

55% males, mean age 52.5 years

97% received angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers, 85% beta-blockers, 98% diuretics

CorCap Cardiac Support Device (CSD)

n = 148

91 received mitral valve repair

Control

n = 152

102 received mitral valve repair

Primary Endpoint

Composite classification of improved, the same, or worse based on occurrence of death, change in NYHA class, or cardiac procedure indicative of heart failure progression.

In the primary composite endpoint, more patients in the CSD group than in the control group were classified as improved, while fewer were classified as worse for a significant odds ratio of 1.73 (p = 0.02).

The primary composite endpoint was largely driven by a significant reduction in major cardiac procedures and a trend toward improvement in NYHA in the CSD group compared with the control group. There was no difference between the two groups in the third component of the primary endpoint, mortality (p = 0.90).

17.1.1.1. Salient findings of the Acorn Trial in the US

- Among patients with heart failure and dilated cardiomyopathy (CMP), the CorCap CSD was associated with a significantly improved primary composite endpoint, namely, clinical status

based on rates of death, major cardiac procedures indicative of heart failure progression, or changes in NYHA class.
- The primary endpoint largely driven by significant reduction in major cardiac procedures and a trend toward improvement in NYHA class in the CSD group. No difference between the two groups in mortality.
- The CSD group had significantly lower left ventricular end-systolic volume (LVESV), left ventricular end-diastolic volume (LVEDV), a significantly greater improvement in sphericity index, and significant improvements in measures of quality-of-life than the control group.
- However, the groups had similar left ventricular (LV) ejection fractions and similar rates of adverse events, including repeat hospitalizations.

17.1.1.1. Drawbacks

Unfortunately, the trial though painted as positive in media releases was turned down by the Food and Drug Administration (FDA) panel. Their reasons were manyfold and make interesting reading:

Lack of complete follow-up
Data not validated by a core lab
Composite endpoint was significant, but no single factor achieved significance of its own
No change in LV ejection fraction between the groups
No differences in heart failure admissions or mortality between the two groups

The decreased need for new cardiac procedures in the study group was perceived as a reluctance on the part of implanting surgeons to go back into a patient with an increased risk of severe adhesions.

While the US experience with the Acorn CorCap was interesting and showed that a randomized multicenter trial could be conducted in cardiac surgery, it also highlighted the need for clear and definite endpoints to be delineated before the study was started.

Another interesting lesson was the Hawthorne effect in all groups that showed that continued care and repeated follow-up actually benefited patients and reduced heart failure symptoms and consequently admissions.

Nevertheless, the areas that showed significant difference were those concerned with LV dimensions and size, with the study group demonstrating that the ventricles were contained at the smaller size. Our own work in animals showed that the best results were obtained when sheep were contained in a moderate phase of heart failure (akin to class II heart failure).[6] Containment late in the cycle of dilatation and heart failure provided marginal benefit with improved survival in sheep with contained ventricles.[8]

In order to make this approach worthy of clinical application, the device has to be dramatically modified to allow subsequent interventions to be safe. In addition, it would be preferable to use smart materials that actively promote reverse remodeling of the ventricles.

17.2. Alteration of Left Ventricular Wall Stress by Shape Change

17.2.1. Myocor Approach

Myocor is a company that started up in 1996 to utilize the concept of ventricular shape alteration to reduce wall stress. It presupposes the left ventricle to be a cylinder or a sphere. If LaPlace's law were applied, wall stress increases proportionate to the radius of curvature. To alter and reduce this, Myocor proposed skewering the heart with a tensioning chord or splint that would change the left ventricle in cross-section from a large circle to two small circles or a bilobed ventricle. Preliminary studies with the Myosplint in human patients were performed in Munich with poor results. McCarthy implanted a few of the myosplint devices acutely in patients undergoing transplantation prior to explant of the heart with similarly poor results.

Figure 17.3 shows the Myocor myosplint, which was an interesting idea but had very few clinical implants.

17.2.2. Cardioclasp

In keeping with the shape change and altering the stresses on the myocardium, Dr David Melvin, from Cincinnati, developed another device that looked and behaved like a vice around the ventricle. This device was named Cardioclasp. While

DropBooks



FIGURE 17.3. The concept behind the Myocor myosplint which alter the short axis of the left ventricle into two bilobed spheres, thereby reducing wall stress.

this concept was interesting, the animal studies showed only mild promise and this concept did not progress to clinical evaluation.

17.2.3. Dynamic Ventricular Restraint (DVR, by CorSet)

The concept of dynamic ventricular restraint was developed by Drs Makkar, Litvak and Eigler at the Cedars Sinai Medical Center, Los Angeles. The concept was tested in animals in Melbourne, Australia, by Raman and colleagues with a prototype restraint device that had inflatable balloon panels along its length, linked to a portacath-type device. The plan was to gradually infuse saline into the portacath so as to slowly increase the constraint over time. Unfortunately, the tubing connecting to the balloons often leaked and there was no indication that the balloons actually inflated enough to cause significant reduction in ventricular size. This device did not proceed beyond initial proof of concept studies in animals. This is quite relevant to the development of other devices by various start-up groups that have touted the benefits of inflatable balloon panels within the pericardium.

17.2.4. Paracor

The concept of dynamic ventricular restraint has been talked about and developed initially by another start-up company called Paracor. This device utilizes a meshwork of nitinol coated with silicone that can be laid around the ventricles to ensure dynamic restraint of the dilating ventricles.

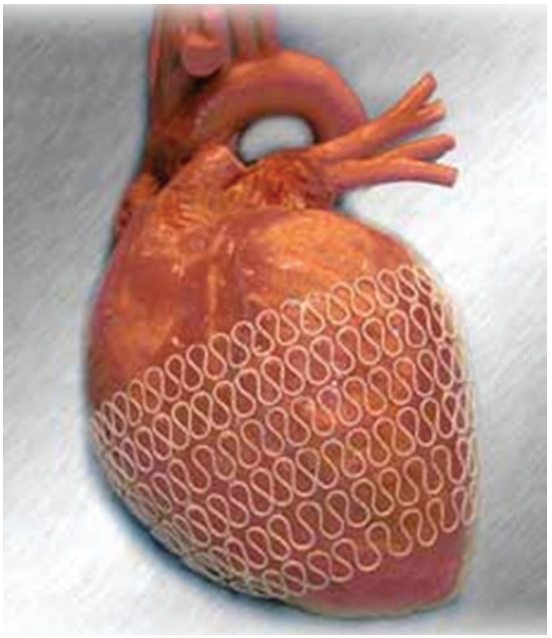


FIGURE 17.4. The Paracor device, which is a nitinol mesh coated with polyurethane and this is slipped over the heart, preventing progressive dilatation.

Figure 17.4 shows the nitinol mesh-based Paracor device implanted around a dilating heart.

There is very little published data about the efficacy of this approach in experimental animals. The first human implant was performed at the Ohio State University on May 19, 2005. Details about this implant are sketchy with a paucity of data in the literature. We await results of this implant experience with interest since nitinol is an alloy that is not immune to fatigue-related stresses.

17.3. Infarct Restraint and/or Constraint

Localized constraint or restraint of dyskinetic or akinetic areas of the ventricles has been studied extensively by Edmunds' laboratory at the University of Pennsylvania. They showed that some kind of nonabsorbable material that is applied and

secured to the epicardial surface of the ventricle in an area of akinetic or dyskinetic scar helps reduce infarct expansion.[9]

Our own adoption of this principle has been in the use of Teflon strips in reinforcing the scar over a reconstructed ventri.cle in the setting of a modified Dor procedure or a LV reconstructive procedure.

17.4. New Devices in the Minimally Invasive Treatment of Mitral Regurgitation

17.4.1. Percutaneous Mitral Valve Approaches

These include a range of devices that straighten or tension up the coronary sinus. These devices are made by many companies such as CDI and Mitralign.

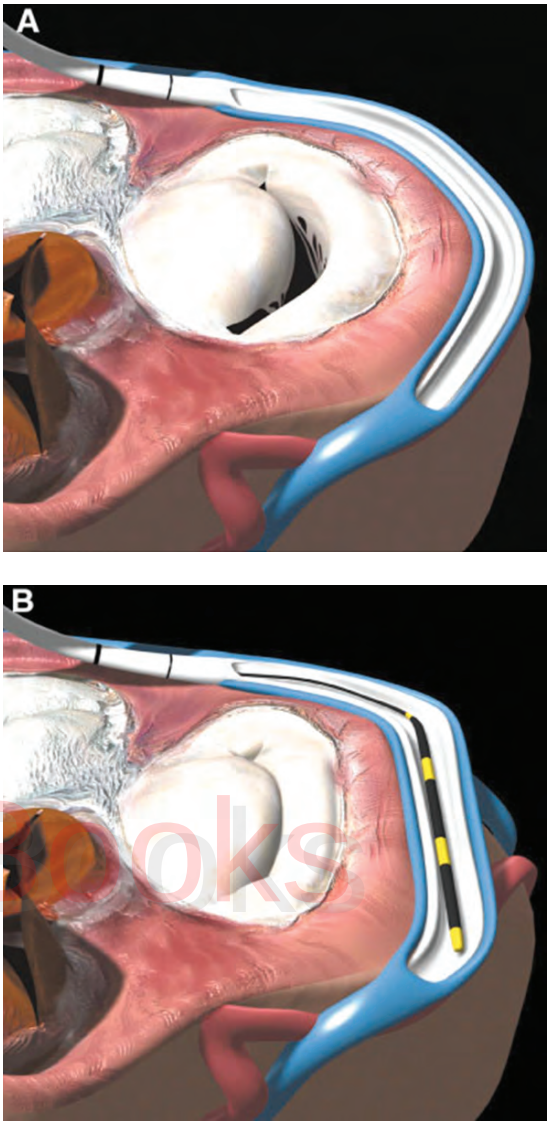
17.4.1.1. Viacor:

Viacor is a start-up company founded by Drs William Cohn and Marc Gillinov, and uses the principle of straightening the coronary sinus to improve mitral valve patency. In experimental animals, especially sheep and pigs, the coronary sinus is large and is more closely applied to the posterior mitral annulus than in humans. In human patients, the coronary sinus is variable in size and in its relationship to the mitral annulus. Hence, the sinus may subtend varying amounts of the muscular portion of the mitral valve annulus. So, a tensioning system or rod in this location has an unpredictable amount of correction of the mitral valve.

Figures 17.5 and 17.6 show a schematic diagram of a coronary sinus-tensioning device. Figure 17.5 shows the sheath in the coronary sinus. The next figure shows the tensioning rod within the coronary sinus sheath.

This approach is flawed for a few reasons:

- The variable relationship and size of the coronary sinus to the muscular portion of the mitral valve annulus.
- Purely annular tightening is not effective in functional or ischemic mitral regurgitation (MR), because the annulus is often normal in size and the mechanism of MR is multifactorial with displacement of papillary muscles, remodeling of the inferobasal region of the left ventricle, dilated ventricles, change in the plane of coaptation of the mitral leaflets to the ventricle, etc.
- The variable relationship of the circumflex coronary artery to the coronary sinus, whereby in a significant number of patients, tensioning the sinus can kink the underlying artery.



FIGURES 17.5–17.6. The sheath in the coronary sinus. Tensioning rod within the coronary sinus sheath. The Viacor device as it tensions up the coronary sinus, in an attempt to correct MR.

DropBooks

17.4.1.2. Carillon (CDI) Device

Figure 17.7 is a schematic diagram of the Cardiac Dimension device. Cardiac Dimensions, Inc., was set up by Clif Alferness, one of the original founders of Acorn Cardiovascular Inc, and the preliminary experimental work was performed by my colleague John Power, at his laboratory in Melbourne, Australia. Limitations of this device are the difficulty in anchoring it to the coronary sinus and the other inherent problems with this approach.

Lack of uniformity in the size of the coronary sinus and variability in its relationship to the muscular portion of the mitral annulus.

The presumption that functional and ischemic MR can be fixed by addressing the annulus, which is often normal in size. Moving the septal and lateral components of the annulus closer to each other can be difficult to achieve with this approach.

Finally, the sheep experiments looking at MR can be erroneous because of poor echocardiographic windows in assessing the degree of MR accurately.

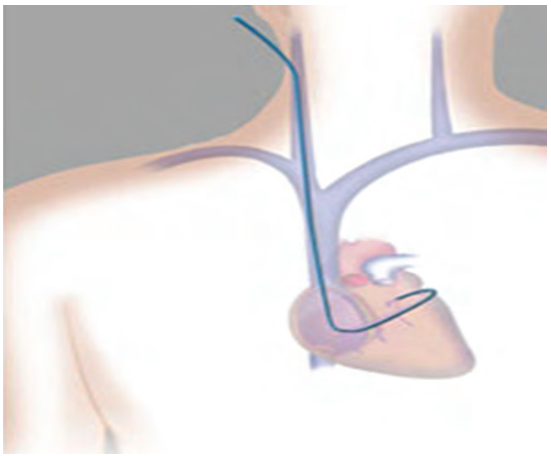


FIGURE 17.7. Schematic diagram of the Cardiac Dimensions device. This diagram shows deployment of the Carillon device, which is deployed in the coronary sinus, and inserted through the jugular vein.

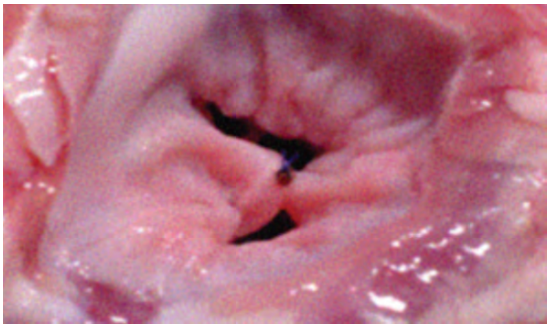


FIGURE 17.8. Edge-to-edge or Alfieri repair: photograph of a clip approximating anterior and posterior mitral leaflets.

Ottavio Alfieri, an innovative surgeon from Milan, suggested the concept of the edge-to-edge mitral valve repair in severely degenerative and myxomatous valves. He utilized the concept of double-orifice mitral valves seen in congenital abnormalities and used sutures to approximate the corresponding portions of anterior and posterior leaflets.[10] However, this is most effective in the presence of an annuloplasty ring. The long-term results of this approach were not very satisfactory in the surgical population. This did not stop the development of this approach by the endovascular route by companies such as E-valve and Edwards. The maximum stress and strain is on the leaflets where they are approximated and this dooms this approach to early failure. Amazingly, despite evidence to the contrary, this device was tested in human patients, partly because it was a minimally invasive procedure and has had poor results. Figure 17.8 shows approximation of the anterior and posterior leaflets with a clip in a pig heart.

17.4.1.3. Coapsys

Myocor then developed a device called Coapsys which is specifically designed to address the subannular component in ischemic MR. This device is deployed using the technology developed by Myocor in skewering the heart and passing a Goretex chord/chords through the ventricle below the level of the mitral annulus with pads on either side. This is at present undergoing a multicenter US trial. Preliminary data from the Escorts Heart Institute in India suggest that this approach of

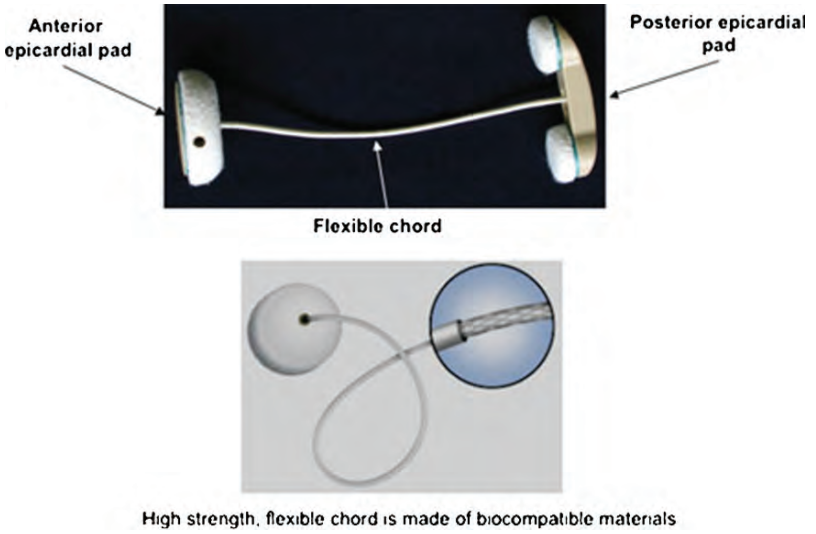

Anterior epicardial pad
Posterior epicardial pad
Flexible chord
High strength, flexible chord is made of biocompatible materials

FIGURE 17.9. Chords that form part of the Coapsys device.

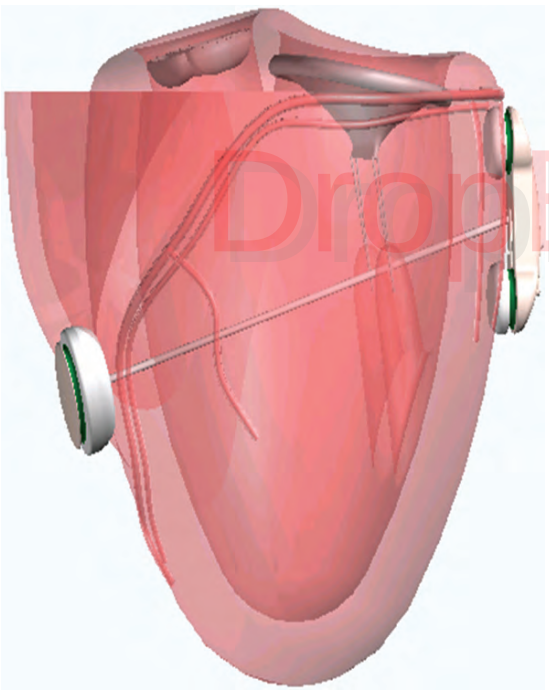


FIGURE 17.10. The deployment of the Coapsys device in longitudinal section of the left ventricle.

skewering the left ventricle below the annulus of the mitral annulus may be effective in some patients with ischemic MR.[11]

Figures 17.9 and 17.10 show the Myocor Coapsys device and its method of deployment.

17.4.1.4. BACE

Basal annuloplasty of the cardia externally (BACE) is a simple concept of externally constraining the base of the ventricles where the mitral and tricuspid valves are subtended.

It is estimated that there are over 2 million people in the USA alone having moderate to severe MR, but only about 100,000 patients undergo valve surgery. Mitral valve reconstructive surgery is now an accepted therapeutic option in heart failure patients with severe MR.[12] However, it is controversial when it comes to moderate MR. In patients with ischemic heart disease and ischemic CMP, evidence is emerging that moderate degrees of MR progress with time and portend an adverse prognosis.[13] Traditionally, mitral valve procedures require access to the mitral valve through an intracavitary approach, which is associated with morbidity and mortality. Mitral valve repair or replacement in the setting of ischemic heart disease carries a mortality risk of between 2% and 6%.[14] A mitral valve procedure along with coronary artery bypass graft (CABG) surgery carries a higher risk of mortality and a definite risk of stroke.[15] This risk profile has made surgeons reluctant to advocate mitral valve repair or replacement unless the degree

of regurgitation is severe. As can be expected, cardiologists are reluctant to refer patients for consideration of a mitral valve reconstructive procedure unless there is evidence of severe mitral insufficiency.

Patients with ischemic heart disease and greater than moderate MR are therefore at a survival disadvantage. We report our experience here with a new procedure of repairing and stabilizing the mitral and tricuspid valves without physically entering the heart.

Study Population. All patients were enrolled at the University of Melbourne Campus Hospitals, Melbourne, Australia.

Three groups of patients undergoing complex cardiac surgery between January 2000 and December 2001 were studied.

A group of 12 patients was enrolled between May 2000 and June 2001 for BACE. These patients had symptomatic triple vessel coronary artery disease and heart failure. They were diagnosed with coronary angiography, radionuclide ventriculography, and were assessed and rated by a cardiologist on the basis of NYHA functional class. The degree of MR was assessed by transthoracic echocardiography before they were referred for surgery.

Patients who had severe MR were excluded from all three groups.

Informed consent was obtained from all patients for the procedure upon clear explanation of the procedure and the risks involved.

The decision to perform BACE was based on preoperative transesophageal echocardiographic (TEE) assessment of MR. Patients in all three groups underwent coronary artery surgery and LV reconstruction, if indicated. In addition, patients in Group 1 underwent external cardiac basal annuloplasty, and patients in Group 2 underwent intracavitary mitral repair.

Surgical Technique:
All procedures were performed through a midline sternotomy incision. The cardiac surgical procedures were performed with the aid of cardiopulmonary bypass (CPB) on a heart arrested by blood cardioplegia.

For patients who were selected for the BACE procedure, soon after the pericardium was opened, the base of the heart was sized and the circumference of the base of the heart was measured. This was done with the heart beating with resting filling pressures, prior to being connected to CPB. The measurement was repeated twice to ensure accuracy. The BACE device was then constructed with a strip of compliant polyester mesh, measuring 4–5 cm in width. The typical length was about 30 cm.

Once the cross-clamp was applied and cardioplegia infused, the heart was lifted up. The BACE device was applied along the atrioventricular groove only along the posterior aspect of the heart. It was then anchored on the atrial and ventricular sides of the atrioventricular groove with 4/0 prolene sutures. The CABGs were then constructed. LV reconstruction was then performed if there were any large confluent ventricular scars that were hemodynamically significant. The cross-clamp was removed, and the heart was allowed to return to a regular rhythm. Once reasonable ventricular contraction was evident on transesophageal echocardiography, attempts were made to wean the patient off CPB.

At this stage, MR was dynamically assessed using TEE. The BACE device was tightened/pulled across just enough to eliminate MR. At this state of tension, the BACE device was then anchored anteriorly and laterally along the atrioventricular groove. The sizing and implantation of the basal annuloplasty device took an average of 20 min.

Figure 17.11 is an operative photograph of the BACE procedure. Figure 17.12 is a schematic diagram of the BACE procedure with support of the annulus and subannular ventricular myocardium.

Patients in Group 2 underwent CABG on pump utilizing a similar technique of CPB and cardioplegic preservation of myocardium. Mitral valve repair was performed with the mitral valve approached through the biatrial transseptal route. The mitral valve was assessed and repaired based on the kind of pathology. A flexible mitral annuloplasty ring was used in all cases.

Patients in Group 3 underwent CABG and/or LV reconstruction. CABG surgery was performed in the standard fashion under cross-clamp and cardioplegia. LV reconstruction was performed in accordance with the principles of geometric endoventricular repair, as described.[16] The aim was to recreate the conical shape of the left ventricle

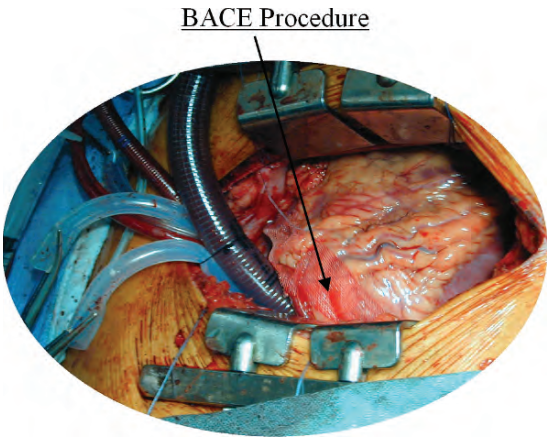


FIGURE 17.11. Basal annuloplasty of the cardia externally (BACE) procedure.

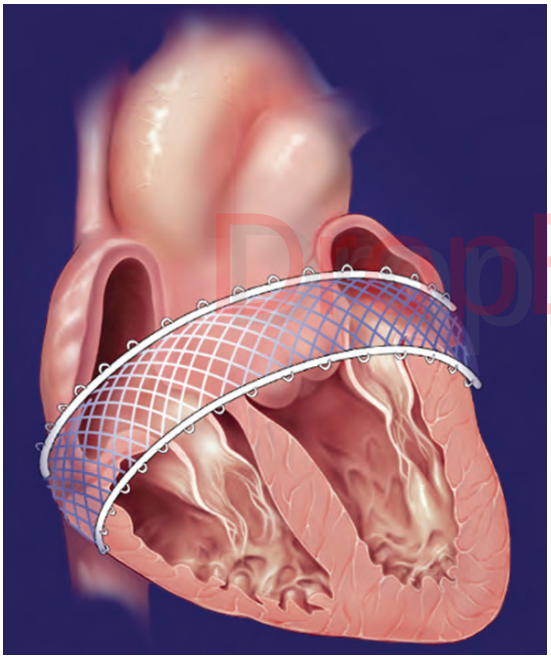


FIGURE 17.12. Schematic diagram of the basal annuloplasty of the cardia externally(BACE) procedure.

with a small patch of bovine pericardium. These patients were operated on an urgent basis. All of them had mild to moderate MR that was left alone in the setting of an urgent operation. Eight of these patients had insertion of intra-aortic balloon pumps perioperatively.

Choice of inotropic support was based on recovery of ventricular function. No intra-aortic balloon pumps were used in the first two groups of patients.

Patients in all three groups were followed up after discharge clinically and echocardiographically every year by a cardiologist.

Results:
There were no perioperative deaths in any group of patients.

Mean number of grafts (CABG) were 3.5 in Group 1 and 3.7 in Group 3. LV reconstruction was performed in 10 of 12 patients in Group 1 and 11 of 12 in Group 3.

Group 2 patients underwent only mitral valve repair. Postoperative stay in the intensive care unit and hospital was similar in all three groups.

There were no intraoperative procedure–related complications in Group 1. There were no significant problems related to the implantation procedure with BACE. All patients in Group 1 were weaned off CPB once they reached trivial to mild MR.

At the follow-up of patients in Group 1, the degree of MR remained stable at trivial to mild (1+ or less, on a grading of 1–4). NYHA functional status improved steadily over the first postoperative year and remained steady at class I. Over the 4 years of clinical follow up, there have been two deaths at the later part of the follow-up period in this group, one from malignancy and one from emphysema. Figure 17.13 shows the improvement of MR that persists at 18 months.

At the follow-up of patients in Group 2, the degree of MR remained at trivial to mild (1+ or less, on a grading of 1–4).

Figure 17.14 shows that there is an improvement in ejection fraction over time. Patients in Group 3 were also followed up over a similar time frame. Functional status improved similarly in this group. However, the degree of MR gradually progressed to a moderate degree of 2.7 (moderate to moderately severe). There were three late deaths in this group, one from sudden death, one from malignancy, and one from pneumonia. Figure 17.15 compares the degree of MR in patients who underwent the BACE procedure with traditional mitral valve repair and those who had LV reconstruction.

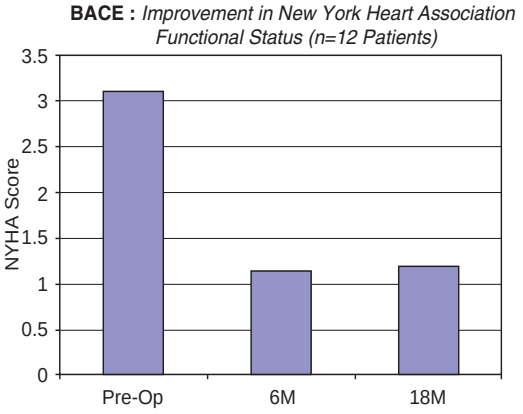


FIGURE 17.13. Basal annuloplasty of the cardia externally (BACE): improvement in NYHA functional status (n = 12 patient).

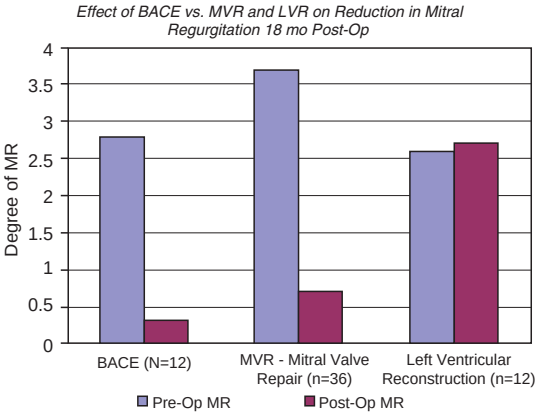


FIGURE 17.15. Effect of basal annuloplasty of the cardia externally (BACE) versus mitral valve repair (MVR) and left ventricular reconstruction (LVR) on reduction in mitral regurgitation 18 months postoperatively.

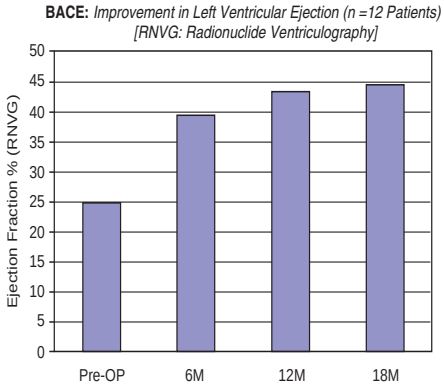


FIGURE 17.14. Basal annuloplasty of the cardia externally (BACE): improvement in left ventricular ejection (n = 12 patients). *RNVG* radionuclide ventriculography.

17.5. Discussion

Regarding the course of action, there is no consensus as far as moderate degree of MR is concerned. Assessment of MR is subjective and can vary depending on a variety of factors ranging from the angle of the transducer[17] to loading conditions and nature of underlying cardiac rhythm[18] to the level of compensation of heart failure. However, the pioneering efforts of echocardiologists like Maurice Enrique-Sarano who have been tireless proponents of objective assessment of MR based on effective regurgitant orifice (ERO) and regurgitant volume are changing the appreciation of MR.[19] This helps in developing a uniform approach to patients with MR. There is now emerging evidence that if severe, even asymptomatic MR is still associated with a bad prognosis.[20] Moderate degrees of MR were often considered fair game for medical therapy. However, there are enough data to show that moderate MR progresses especially in patients with ischemic heart disease and is associated with adverse outcomes.[21] The only definitive methods of dealing with MR are intracavitary operative procedures that either repair the annulus of the mitral valve or replace the mitral valve with a prosthetic valve. Since both are major cardiac surgical procedures performed with the aid of CPB and cardioplegic arrest, there are significant associated complications and risks. Traditionally, combined coronary artery bypass and mitral valve surgery have been associated with a significant morbidity and mortality.[22] As a result, cardiologists have been reluctant to refer patients for these procedures, and surgeons, on the other hand, have viewed these combined operations with trepidation.

17.6. Conclusions

This report shows that external stabilization of the cardiac base with BACE can effectively work like an annuloplasty of the mitral valve while providing support to the ventricular myocardium below the annulus of the valve. In addition, the tricuspid

valve is also supported. Since the procedure was performed in a high-risk population with no major perioperative complications, it appears to be a worthwhile approach to undertake.

The advantages are the following:

- the application is external; therefore the complications associated with intracavitary approach such as endocarditis, coagulopathies, and so on can potentially be avoided
- opportunity for the dynamic assessment of the valves while tightening the BACE device
- support of the ventricular myocardium below the annulus
- possibility of implanting the device off-pump or on a beating heart

17.7. Keypoints to Remember

Containment of ventricles is an important and interesting way of limiting progressive dilatation of the heart. However, this technique is best developed with a nonreactive material and has potential in slowly reducing the size of the heart.

Shape change by other means such as those proposed by Myocor and Cardioclasp while reducing wall stress in theory have not translated into clinical trials.

Percutaneous approaches to the mitral are interesting and we await their results in human trials. MR due to ventricular dilatation is multifactorial and needs careful planning before executing some kind of surgical reparative procedure.

Annular support along with some kind of means of favorable deformation of the adjacent myocardium externally may be an exciting way forward in performing mitral valve repair without entering the heart.

The future of shape change of the ventricles will probably incorporate some kind of cellular therapy.

References

1. Frank O. (1895). On the dynamics of cardiac muscle. Wasserman E (1959), trans. *Am Heart J*. 1959;58:282-317.
2. Patterson SW, Starling EH. On the mechanical factors which determine the output of the ventricles. *J Physiol*. 1914;48:357-379.
3. Guccione JM, McCullouch AD. Passive material properties of intact ventricular myocardium determined from a cylinder model. *ASME J Biomech Eng*. 1991;113:42-55.
4. Freeman GL, LeWinter MM. Pericardial adaptations during chronic cardiac dilation in dogs. *Circ Res*. 1984;54:294-300.
5. Power JM, Raman J, Dornom A, Farish SJ, Burrell, Tonkin AM, Buxton B, Alferness A. Passive ventricular constraint amends the course of heart failure: a study in an ovine model of dilated cardiomyopathy. *Cardiovasc Res*. 1999;44:549–55.
6. Raman JS, Byrne MJ, Power JM, Alferness CA. Ventricular constraint in severe heart failure halts decline in cardiovascular function associated with experimental dilated cardiomyopathy. *Ann Thorac Surg*. 2003 Jul;76(1):141–7.
7. Sabbah HN, Sharov VG, Gupta RC, Mishra S, et al. Reversal of chronic molecular and cellular abnormalities due to heart failure by passive ventricular containment. *Circ Res*. 2003;93(11):1095–101.
8. Raman J, Hata M, Storer MM. Hare DL, Buxton BF: The mid-term results of ventricular containment (Acorn Wrap) for end-stage ischemic cardiomyopathy. *Ann Thorac Cardiovasc Surg*. 2001;7:278–81.
9. Moainie SL, Guy TS, Gorman JH 3rd, Plappert T, Jackson BM, St John-Sutton MG, Edmunds LH Jr, Gorman RC. Infarct restraint attenuates remodeling and reduces chronic ischemic mitral regurgiration after posterolateral infarction. *Ann Thorac Surg.* 2002;74(2):444–9.
10. Maisano F, Torraca L, Oppizzi LM, Stefano PL, D'Addario, Alfieri O. The edge-to-edge technique: a simple method to correct mitral insufficiency. *Eur J Cardiothorac Surg*. 1998;13(5):240–5.
11. Mishra YK, Mittal S, Jaguri P, Trehan N. Coapsys mitral annulus for chronic ischemic mitral regurgitation: 1 year results. *Ann Thorac Surg.* 2006;81(1): 42–6.
12. Bolling SF. Mitral reconstruction in cardiomyopathy. *J Heart Valve Dis*. 2002;11(suppl 1):S26-S31.
13. Trichon BH, Felker GM, Shaw LK, Cabell CH, O'Connor CM. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. *Am J Cardiol*. 2003;91(5):538-543.
14. Mantovani V, Mariscalco G, Leva C, Blanzola C, Cattaneo P, Sala A. Long-term results of the surgical treatment of chronic ischemic mitral regurgitation: Comparison of repair and prosthetic replacement. *J Heart Valve Dis*. 2004;13(3): 421–428; discussion 428-429.
15. Tsialtas D, Bolognesi R, Reverberi C, Beghi C, Manca C, Gherli T. Surgical coronary revascularization with or without mitral valve repair of severe ischemic dilated cardiomyopathy. *Heart Surg Forum*. 2005;8(3):E146-E150.

DropBooks

16. Raman J, Sakaguchi G, Buxton BF, Outome of geometric endoventricular repair in impaired left ventricular function. *Ann Thorac Surg*. 2000;70:1127–1129.
17. Gottdiener JS, Panzer JA, St John Sutton M, Bannon P, et al. Testing the test: The reliability of echocardiography in the sequential assessment of valvular surgery. *Am Heart J* 2002;144(1):115-121.
18. Weissman NJ, Panzer JA, Tighe JF Jr, et al. Specificity of Doppler Echocardiography for the assessment of changes in valvular regurgitation: Comparison of side-by-side versus serial interpretation. *J Am Coll Cardiol*. 2001;37(6):1614-1621.
19. Enrique-Sarano M, Freeman WK, Tribouilloy CM, Orszulak TA, et al. Functional anatomy of MR: Accuracy and outcome implication of TEE. *J Am Coll Cardiol*. 1999;34(4):1129-1136.
20. Enriquez-Sarano M, Avierinos JF, Messika-Zeitoun D, Detaint D, et al. Quantitative determinants of the outcome of asymptomatic mitral regurgitation. *N Eng J Med*. 2005;352(9):875–83.
21. Picard MH, Davidoff R, Sleep LA, et al. Echocardiographic predictors of survival and response to early revascularization in cardiogenic shock. *Circulation*. 2003;107(2):279-284.
22. Ambler G, Omar RZ, Royston P, Kinsman R, Keogh BE, Taylor KM. Generic, simple risk stratification model for heart valve surgery. *Circulation*. 2005;112(2): 224-231.

18
Other Techniques in Special Circumstances: Pulmonary Thromboendarterectomy in Right Heart Failure

Michael M. Madani and Stuart W. Jamieson

18.1. Introduction

Pulmonary thromboendarterectomy (PTE) is the definitive treatment for chronic pulmonary hypertension as the result of thromboembolic disease and is now widely recognized as the treatment of choice for patients suffering from right heart failure as the result of chronic thromboembolic pulmonary hypertension (CTEPH). Although the procedure is curative and in experienced hands carries a low morbidity and mortality, it is rarely performed. The main problem is the fact that CTEPH remains significantly under-recognized. It is not uncommon for the patients suffering from this disease to be misdiagnosed and mistreated for a variety of other conditions. Furthermore, of those who are truly diagnosed, the majority will be at late stages of the disease. However, once correctly diagnosed and referred, PTE can be highly effective and promises to provide a lifetime cure for such patients.

Unlike other forms of heart failure, patients with CTEPH often have full recovery of their right heart function and size, as long as the pulmonary hypertension has resolved. This is an interesting and unexplained phenomenon that is a unique feature of the right heart failure associated with CTEPH. In most other causes of heart failure, especially left ventricular failure, even when the obstruction has been removed, the ventricle does not fully recover and certainly does not normalize in size. In contrast, in the setting of CTEPH, the right ventricle does so. The improvement in right heart failure and its associated tricuspid regurgitation is proportional to the degree of resolution achieved in the patient's pulmonary hypertension. Therefore one can expect full recovery of the right heart and normal tricuspid function in patients who have had successful outcomes with normal postoperative pulmonary pressures.

Pulmonary hypertension and subsequent right heart failure secondary to chronic thromboembolic disease is a relatively uncommon condition occurring in 1–5% of adult patients who survive an acute pulmonary embolic event.[1,2] More recent studies, however, suggest a higher incidence in patients with an acute episode of pulmonary embolism; 3.1% at 1 year and 3.8% at 2 years.[2,3] It is extremely hard to accurately determine the true incidence of CTEPH for obvious reasons, but one can come up with educated estimates of this disease. The estimated incidence of acute pulmonary embolism is ~630,000 per year in the United States, based on clinical data,[4,5] and is related to ~235,000 deaths per year, based on autopsy data.[6] Calculations extrapolated from mortality rates and the random incidence of major thrombotic occlusion of pulmonary vessels at autopsy support an estimate that more than 100,000 people in the United States currently suffer from pulmonary hypertension that could be relieved by operation.[7]

Once chronic pulmonary hypertension develops, the prognosis is poor, and this prognosis is even worse in patients without an intracardiac shunt. As a rule, patients with pulmonary hypertension caused by pulmonary emboli fall into a higher risk category than those with Eisenmenger's syndrome and encounter a higher mortality rate. In fact, survival of patients with CTEPH is inversely related to the

DropBooks

magnitude of pulmonary artery systolic pressure and pulmonary vascular resistance.[8] When the mean pulmonary artery pressure in patients with thromboembolic disease exceeds 50 mmHg, the 5-year mortality approaches 90%.[9]

Regardless of the exact incidence or the circumstances, it is clear that acute embolism and its chronic relation, fixed chronic thromboembolic occlusive disease, are both much more common than generally appreciated and are seriously underdiagnosed. Houk and colleagues[10] in 1963 reviewed the literature of 240 reported cases of chronic thromboembolic obstruction of major pulmonary arteries but found that only 6 cases had been diagnosed correctly before death. Calculations extrapolated from mortality rates and the random incidence of major thrombotic occlusion found at autopsy would support a postulate that more than 100,000 people in the United States currently have pulmonary hypertension that could be relieved by operation. Therefore, despite an improved understanding of pathogenesis, diagnosis, and management, pulmonary emboli and the long-term sequelae of thromboembolic pulmonary hypertension remain frequent and often fatal disorders.

18.2. Clinical Presentation

There are no signs or symptoms specific for chronic thromboembolism. The most common symptom associated with thromboembolic pulmonary hypertension, as with all other causes of pulmonary hypertension and right heart failure, is exertional dyspnea. This dyspnea is out of proportion to any abnormalities found on clinical examination. Like complaints of easy fatigability, dyspnea that initially occurs only with exertion is often attributed to anxiety or being "out of shape." Syncope, or presyncope (light-headedness during exertion), is another common symptom in pulmonary hypertension. Generally, it occurs in patients with more advanced disease and higher pulmonary arterial pressures.

Nonspecific chest pains or tightness occur in 50% of patients with more severe pulmonary hypertension. Hemoptysis can occur in all forms of pulmonary hypertension and probably results from abnormally dilated vessels distended by increased intravascular pressures. Peripheral edema, early satiety, and epigastric or right upper quadrant fullness or discomfort will develop as the right heart failure progresses. Some patients with chronic pulmonary thromboembolic disease present after a small acute pulmonary embolus that may produce acute symptoms of right heart failure. A careful history brings out symptoms of dyspnea on minimal exertion, easy fatigability, diminishing activities, and episodes of angina-like pain or light-headedness. Further examination reveals the signs of pulmonary hypertension and right heart failure.

The physical signs of pulmonary hypertension are the same no matter what the underlying pathophysiology. Initially the jugular venous pulse is characterized by a large A-wave. As the right heart fails, the V-wave becomes predominant. The right ventricle is usually palpable near the lower left sternal border, and pulmonary valve closure may be audible in the second intercostal space. Occasional patients with advanced disease are hypoxic and slightly cyanotic. Clubbing is an uncommon finding.

The second heart sound is often narrowly split and varies normally with respiration; P2 is accentuated. A sharp systolic ejection click may be heard over the pulmonary artery. As the right heart fails, a right atrial gallop usually is present, and tricuspid insufficiency develops. Because of the large pressure gradient across the tricuspid valve in pulmonary hypertension, the murmur is high pitched and may not exhibit respiratory variation. These findings are quite different from those usually observed in tricuspid valvular disease. A murmur of pulmonic regurgitation may also be detected.

18.3. Diagnosis

To ensure diagnosis in patients with right heart failure secondary to chronic pulmonary thromboembolism, a standardized evaluation is recommended for all patients who present with unexplained pulmonary hypertension. This workup includes a chest radiograph, which may show either apparent vessel cutoffs of the lobar or segmental pulmonary arteries or regions of oligemia suggesting vascular occlusion. Central pulmonary arteries are generally enlarged, and the right ventricle may also be enlarged without any enlargement of the left atrium or ventricle. However, one should keep

in mind that despite these classic findings, a large number of patients might present with a relatively normal chest radiograph, even in the setting of high degrees of pulmonary hypertension or right heart failure. The electrocardiogram demonstrates findings of right ventricular hypertrophy (right axis deviation, dominant R-wave in V1). Pulmonary function tests are necessary to exclude obstructive or restrictive intrinsic pulmonary parenchymal disease as the cause of the hypertension.

The most useful screening studies are two-dimensional surface echocardiography with Doppler imaging and ventilation-perfusion (V/Q) scanning. The standard echo helps to define the presence and severity of right heart failure, tricuspid regurgitation, and severity of pulmonary hypertension. In addition it is also helpful to rule out certain other causes, such as Eisenmenger's syndrome. The echocardiogram rapidly demonstrates right-sided chamber enlargement and right ventricular hypertrophy (Figure 18.1). The main pulmonary artery is usually enlarged; the intraventricular septum may appear flattened and often exhibits paradoxical motion, with encroachment of the right ventricular septum in the left ventricle. Varying degrees of tricuspid regurgitation are usually present. Continuous wave Doppler scanning of the tricuspid regurgitation jet is helpful in the estimation of the pulmonary artery systolic pressure. In addition, because exercise characteristically increases the pulmonary hypertension, echocardiography with exercise should always be applied whenever the disease is suspected but when the resting echocardiogram demonstrates only subtle abnormalities.

The ventilation-perfusion lung scan is the fundamental test for establishing the diagnosis of unresolved pulmonary thromboembolism. An entirely normal lung scan excludes the diagnosis of both acute and chronic, unresolved thromboembolism. The usual lung scan pattern in most patients with primary pulmonary hypertension either is relatively normal or shows a diffuse nonuniform perfusion. When subsegmental or larger perfusion defects are noted on the scan, even when matched with ventilatory defects, pulmonary angiography is appropriate to confirm or rule out thromboembolic disease.

Currently, pulmonary angiography still remains the gold standard for diagnosis of CTEPH; however,

DropBooks

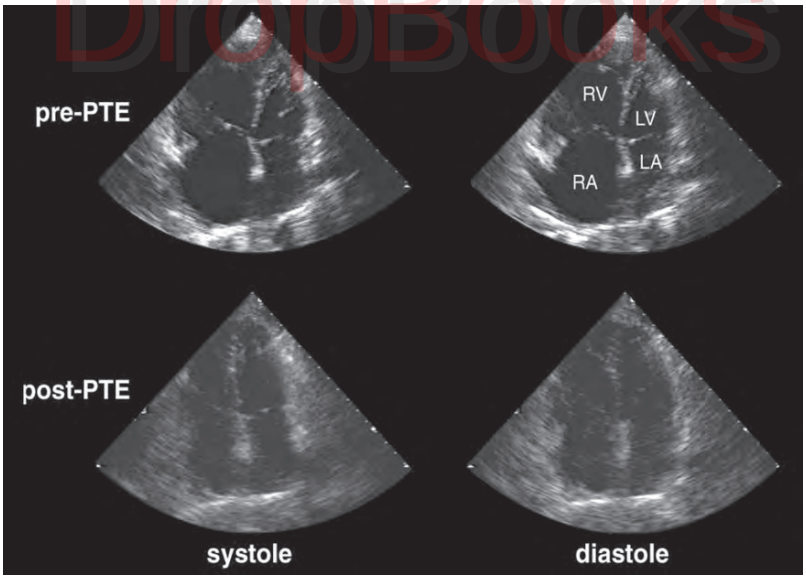


FIGURE 18.1. Echocardiographic appearances of the heart before (pre-pulmonary thromboendarterectomy, PTE; top) and after (post-PTE; bottom) operation. Note the shift of the intraventricular septum toward the left in systole before the operation (top left), together with the relatively small left atrial and left ventricular chambers. After the operation, the septum is restored to its normal geometry, and the massive enlargement of the right atrium and the right ventricle has resolved.

with the advent of high resolution scans and magnetic resonance imaging, more and more centers rely on the diagnostic power and the noninvasive nature of these tests to confirm the diagnosis. Organized thromboembolic lesions do not have the appearance of the intravascular filling defects seen with acute pulmonary emboli, and experience is essential for the proper interpretation of pulmonary angiograms in patients with unresolved, chronic embolic disease. Organized thrombi appear as unusual filling defects, webs, or bands, or completely thrombosed vessels that may resemble congenital absence of the vessel[11] (Figure 18.2). In addition to pulmonary angiography, patients over 45 undergo coronary arteriography and other cardiac investigation as necessary. If significant disease is found, additional cardiac surgery is performed at the time of PTE.

In recent years higher resolution helical computed tomography (CT) scans of the chest have been used more frequently in diagnosis of pulmonary thromboembolic disease. Presence of large clots in lobar or segmental vessels generally confirms the diagnosis. CT features of CTEPH include evidence of organized thrombus lining the pulmonary vessels in an eccentric fashion, enlargement of the right ventricle and the central arteries, variation in size of segmental arteries, and parenchymal changes characteristic of pulmonary infarction. In addition, in rare situations where there are concerns of external compression, or occlusion of main pulmonary arteries are present, CT scans can be helpful in differentiating thromboembolic disease from other causes such as mediastinal fibrosis, lymph nodes, or tumors. In the current era of multidetector CT scans, the resolution of the pulmonary arteries is much better and it is very likely that this diagnostic modality will soon replace pulmonary angiography as the gold standard in diagnosing CTEPH and in planning the surgical treatment once the diagnosis is made. In addition, the volumetric assessment of the right ventricle can be more accurately performed with multidetector CT.

18.4. Medical Treatment

There is no curative role for medical management of these patients and at best it is palliative. There are a number of new pulmonary vasodilators that are now available for the treatment of the pulmonary hypertension and right heart failure in these patients, but considering the fact that the primary pathology

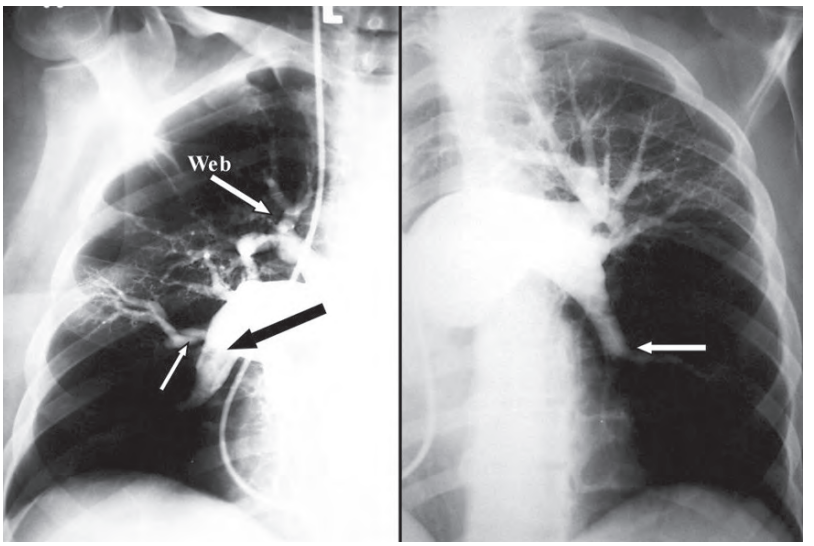


FIGURE 18.2. Pulmonary angiogram in a patient with chronic thromboembolic pulmonary hypertension. Please note the extensive areas of hypoperfusion as a result of complete occlusion, as well as luminal irregularities, webs, bands, and pouches, shown by arrows.

is the physical obstruction of pulmonary vasculature, there is no surprise that their effects are only transient at best. Right ventricular failure may show some improvement with combination of diuretics and vasodilators, but because the failure is due to a mechanical obstruction it will not resolve until the obstruction is removed. Similarly, the prognosis is unaffected by medical therapy,[12,13] which should be regarded as only supportive. Because of the bronchial circulation, pulmonary embolization seldom results in tissue necrosis. Surgical endarterectomy therefore will allow distal pulmonary tissue to be used once more in gas exchange.

Chronic anticoagulation represents the mainstay of the medical regimen. Anticoagulation is primarily used to prevent future embolic episodes, but it also serves to limit the development of thrombus in regions of low flow within the pulmonary vasculature. Inferior vena caval filters are used routinely to prevent recurrent embolization.

18.5. Operative Procedure

PTE is a technically demanding operation that is performed only in select centers around the world. Proper patient selection, meticulous surgical technique, and vigilant postoperative management have contributed to the success of this operation. A true endarterectomy (not an embolectomy) of all affected parts of the lung is essential to clear all affected areas of the pulmonary vasculature. It is clear that pulmonary endarterectomy relieves pulmonary hypertension by improving lung ventilation-perfusion match, improving right ventricular function and tricuspid regurgitation, limiting retrograde extension of clot obstruction, and preventing arteriopathic changes in the remaining patent small pulmonary vessels.[14,15] Furthermore, with resolving pulmonary hypertension, the right ventricle will regress to a normal size and improve its overall function.

The description of a surgical procedure for removal of thromboembolic material dates back to 1908, when Trendelenburg[16] first illustrated an approach in a dying patient. However, it was not until the introduction and development of cardiopulmonary bypass when more procedures with better outcomes were performed. By the mid-1980s there were a total of 85 reported cases that were managed surgically but still carried a high mortality rate of about 22%.[17] Although there have been other reports of surgical treatment of CTEPH, most of the surgical experience in pulmonary endarterectomy has been reported from the University of California, San Diego (UCSD) Medical Center,[7,11] and it is this experience that forms the basis of this chapter.

With our growing experience now accounting for over 2000 of these procedures, we know that there are certain principles of this procedure that have to be adhered to. Although an endarterectomy is possible even if one deviates from these principles, a successful and complete endarterectomy is not, and such outcomes are questionable. What follows is a description of the techniques of this procedure highlighting the fundamental points.

18.6. Technical Principles of the Procedure

There are several guiding principles for this operation. First and foremost the approach must be bilateral, because, for pulmonary hypertension to be a major factor, both pulmonary arteries must be substantially involved. Furthermore, it is extremely unlikely to have unilateral disease as the result of thromboembolism. In fact we believe that a small subgroup of our patients who truly do have unilateral disease perhaps suffer from an underlying pulmonary vascular pathology with subsequent thrombosis rather than true thromboembolism. The only reasonable approach to both pulmonary arteries is through a median sternotomy incision. Historically, there have been many reports of unilateral operation, and occasionally this is still performed with various results in inexperienced centers, through a thoracotomy. However, the unilateral approach ignores the disease on the contralateral side, subjects the patient to hemodynamic jeopardy during the clamping of the pulmonary artery, and does not allow good visibility because of the continued presence of bronchial blood flow. In addition, collateral channels develop in chronic thrombotic hypertension not only through the bronchial arteries but also from diaphragmatic, intercostal, and pleural vessels. The dissection of the lung in the pleural space via a thoracotomy incision can therefore be extremely bloody. The median

DropBooks

sternotomy incision, apart from providing bilateral access, avoids entry into the pleural cavities, and allows the ready institution of cardiopulmonary bypass.

Cardiopulmonary bypass is an essential part of this operation and integral to ensure cardiovascular stability during the procedure. In addition cardiopulmonary bypass allows cooling the patient in preparation of circulatory arrest. Given the extent and the location of thromboembolic material, which has now transformed into a scar-like fibrotic tissue adherent to the pulmonary vasculature, superior visibility is required. This is achievable only in a bloodless field, so the surgeon can define an adequate endarterectomy plane and then can follow the pulmonary endarterectomy specimen deep into the subsegmental vessels. Because of the copious bronchial blood flow usually present in these patients, periods of circulatory arrest are necessary to ensure perfect visibility. Again, there continue to be sporadic reports of performing this operation without circulatory arrest with various outcomes. However, it should be emphasized that although endarterectomy is clearly possible without circulatory arrest, a complete endarterectomy is not. Surgeons claiming success with a complete endarterectomy without circulatory arrest are likely to leave behind distal disease in the subsegmental branches without ever recognizing it. We always initiate the procedure without circulatory arrest, and depending on the collateral flow through the bronchial arteries and other channels, a variable amount of dissection is possible before the circulation has to be stopped, but never a complete dissection. The circulatory arrest periods are typically limited to 20 min, with restoration of flow between each arrest. With experience, a complete endarterectomy usually can be performed within a single period of circulatory arrest on each side.

The next principle of this operation relies mainly on the experience of the operator in recognizing the true endarterectomy plane of the media, and following the specimen to its feathered tail end in each branch. It is essential to appreciate that the removal of visible thrombus is largely incidental to this operation. Indeed, in most patients, no free thrombus is present, and on initial direct examination, the pulmonary vascular bed may appear normal. The early literature on this procedure indicates that thrombectomy was often performed without endarterectomy, and in these cases the pulmonary artery pressures did not improve, often with the resultant death of the patient.

18.7. Surgical Technique

The surgical approach for this procedure is through a median sternotomy to gain access to both sides. Typically the right heart is severely enlarged, with a tense right atrium and a variable degree of tricuspid regurgitation. There is usually significant right ventricular hypertrophy and associated right heart failure, and with critical degrees of obstruction, the patient's condition may become unstable with the manipulation of the heart. Care must be taken to avoid any unnecessary manipulation of the heart while the patient is safely placed on cardiopulmonary bypass.

Anticoagulation is achieved with the use of heparin sodium (400 units/kg, intravenously) administered to prolong the activated clotting time beyond 400 s. Full cardiopulmonary bypass is instituted with high ascending aortic cannulation and two caval cannulae. The heart is emptied on bypass, and a temporary pulmonary artery vent is placed in the midline of the main pulmonary artery about 1 cm distal to the pulmonary valve. The insertion site can then be used for the beginning of the left pulmonary arteriotomy. The patient is then actively cooled to a core temperature of about 18–20 °C.

Initially, it is most convenient for the primary surgeon to stand on the patient's left side, and perform the endarterectomy on the right side. The superior vena cava (SVC) is also fully mobilized. The approach to the right pulmonary artery is made medial, not lateral, to the SVC. Once the SVC is fully mobilized, and the core temperature has reached 20 °C, an aortic cross-clamp is applied and myocardial protection is provided through a single dose of antegrade cold blood cardioplegia (1 L). The entire procedure is now performed with a single aortic cross-clamp period with no further administration of cardioplegic solution. Additional myocardial protection is provided by using a cooling jacket surrounding the heart throughout the remainder of the procedure. Both tourniquets are now secured around the superior and inferior vena cavae to ensure complete drainage and to avoid any

air entry in the venous cannulae during circulatory arrest.

A modified cerebellar retractor is then used to expose the pulmonary artery between the aorta and the SVC. An incision is made in the right pulmonary artery from beneath the ascending aorta out under the SVC and entering the lower lobe branch of the pulmonary artery just after the take-off of the middle lobe artery (Figure 18.3). It is important that the incision stays in the center of the vessel and continues in the middle of the descending pulmonary artery into the lower, rather than the middle, lobe artery. The incision is carried past the take-off of the middle lobe artery.

Any loose thrombus, if present, is now removed. This is necessary to obtain good visualization. It is most important to recognize, however, that first, an embolectomy without subsequent endarterectomy is quite ineffective and, second, that in most patients with chronic thromboembolic hypertension, direct examination of the pulmonary vascular bed at operation generally shows no obvious embolic material. Therefore, to the inexperienced or cursory glance, the pulmonary vascular bed may well appear normal even in patients with severe chronic embolic pulmonary hypertension.

If the bronchial circulation is not excessive, the endarterectomy plane can be found during this early dissection. However, although a small amount of dissection can be performed before the initiation of circulatory arrest, it is unwise to proceed unless perfect visibility is obtained because the development of a correct plane is essential.

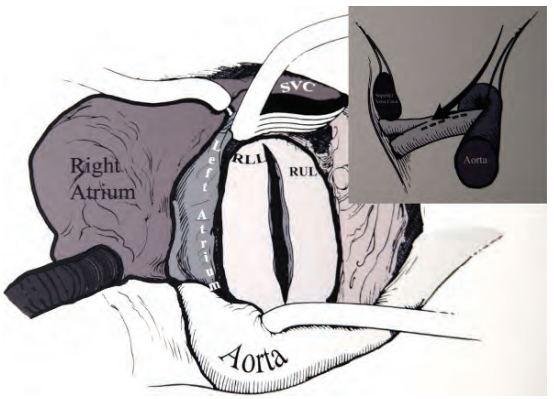


FIGURE 18.3. Exposure of the right pulmonary artery, as viewed by the surgeon standing on the left side. The incision is placed between the superior vena cava (SVC) and the aorta, as shown in the inset. It is imperative that the incision toward the right lower lobe artery is made in the middle of the vessel. During the dissection the edges of this incision are left intact for easier and more hemostatic closure.

The correct plane appears pearly white which is smooth and silky in appearance and lies between the intima and media. A microtome knife is used to develop the endarterectomy plane posteriorly, because any inadvertent egress in this site could be repaired readily, or simply left alone. Dissection in the correct plane is critical because if the plane is too deep the pulmonary artery may perforate, with fatal results, and if the dissection plane is not deep enough, inadequate amounts of the chronically thromboembolic material will be removed. When the proper plane is entered, the layer will strip easily, and the material left with the outer layers of the pulmonary artery will appear somewhat yellow, but there should be no residual yellow plaque.

If the dissection is too deep, a reddish or pinkish color indicates the adventitia has been reached. As a general rule while developing the plane of dissection a nonsmooth light purplish or pinkish color is an indication that the plane of dissection is too deep and care must be taken to immediately get back into the more superficial correct plane before the vessel wall is injured. Once the correct plane is recognized the dissection is carried into each one of the lobar, segmental, and subsegmental branches until a feathered tail is obtained.

There are four broad types of pulmonary occlusive disease related to thrombus that can be appreciated, and we use the following classification[11]: type I disease (~20% of cases of thromboembolic pulmonary hypertension; Figure 18.4) refers to the situation in which major vessel clot is present and readily visible on the opening of the pulmonary arteries. In type II disease (~60% of cases; Figure 18.5), no major vessel thrombus can be appreciated. In these cases only thickened intima can be seen, occasionally with webs, and the endarterectomy plane is raised in the main, lobar, or segmental vessels. Type III disease (~20% of cases; Figure 18.6) presents the most challenging surgical situation. The disease is very distal and confined to the segmental and subsegmental branches. Type III disease is most often associated with presumed repetitive thrombi from indwelling catheters (such as pacemaker wires) or ventriculoatrial

DropBooks

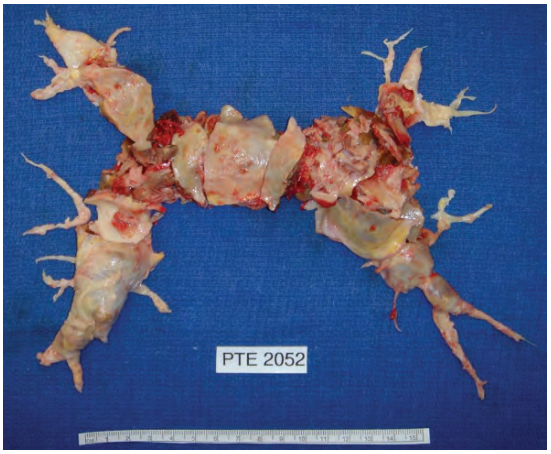


FIGURE 18.4. Surgical specimen removed from right and left pulmonary arteries. Fresh thrombus in major arteries indicates type I disease. Note that removal of only the fresh material leaves a large amount of disease behind. The ruler measures 15 cm.

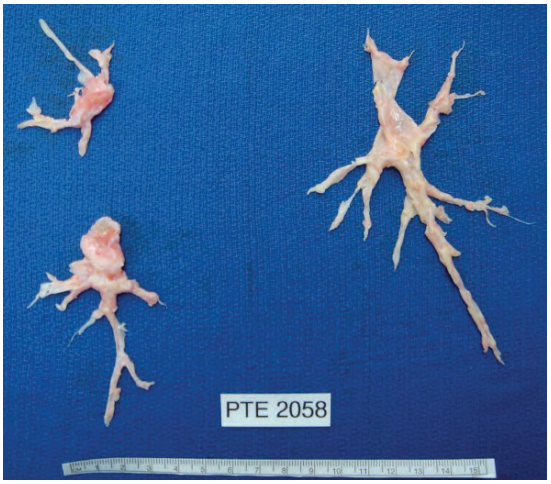


FIGURE 18.5. Surgical specimen removed from right and left pulmonary arteries indicating evidence of type II disease. There are no fresh thromboembolic material in this specimen, but there is evidence of old clots in the lobar and segmental branches. Note the extent of dissection down to the tail end of each one of the branches. The ruler measures 15 cm.

shunts. Type IV disease does not represent primary thromboembolic pulmonary hypertension and is inoperable. In this entity there is intrinsic small-vessel disease, although secondary thrombus may occur as a result of stasis. Small-vessel disease may



FIGURE 18.6. Surgical specimen removed from right and left pulmonary arteries in a patient with type III disease. Note that in this patient the dissection plane has to be developed and raised at each segmental level. The ruler measures 15 cm.

be unrelated to thromboembolic events ("primary" pulmonary hypertension) or occur in relation to thromboembolic hypertension as a result of a high-flow or high-pressure state in previously unaffected vessels similar to the generation of Eisenmenger's syndrome. We believe that there may also be sympathetic "cross-talk" from an affected contralateral side or stenotic areas in the same lung.

With the modified cerebellar retractor in place and the artery well exposed, the dissection is then carried on. When blood obscures direct vision of the pulmonary vascular bed, circulatory arrest is then initiated, and the patient undergoes exsanguination. It is rare that one 20-min period for each side is exceeded.

The endarterectomy is then performed with an eversion technique. Because the vessel is everted and subsegmental branches are being worked on, a perforation here will become completely inaccessible and invisible later. This is why the absolute visualization in a completely bloodless field provided by circulatory arrest is essential. It is important that each subsegmental branch is followed and freed individually until it ends in a "tail," beyond which there is no further obstruction. Residual material should never be cut free; the entire specimen should "tail off" and come free spontaneously.

Once the right-sided endarterectomy is completed, circulation is restarted, and the arteriotomy is repaired with a continuous 6-0 polypropylene suture. The hemostatic nature of this closure is aided by the nature of the initial dissection, with the full thickness of the pulmonary artery being preserved immediately adjacent to the incision.

After the completion of the repair of the right arteriotomy, the surgeon moves to the patient's right side.

The left-sided dissection is virtually analogous in all respects to that accomplished on the right. The duration of circulatory arrest intervals during the performance of the left-sided dissection is subject to the same restriction as the right.

After the completion of the endarterectomy, cardiopulmonary bypass is reinstituted and warming is commenced. The rewarming period generally takes ~90–120 min but varies according to the body mass of the patient.

On the basis of the results of the preoperative echo and the intraoperative TEE, we would then decide if a right atrial exploration is necessary. In general, if either one of the two test is positive for a bubble test we would explore the right atrium. The right atrium is then opened through a small atriotomy located over the site of fossa ovalis. Any intra-atrial communication is then closed. Although tricuspid valve regurgitation is invariable in these patients and is often severe, tricuspid valve repair is not performed. Right ventricular remodeling occurs within a few days, with the return of tricuspid competence.

If other cardiac procedures are required, such as coronary artery or mitral or aortic valve surgery, these are conveniently performed during the systemic rewarming period.[14]

When the patient has fully rewarmed, cardiopulmonary bypass is discontinued. Dopamine is routinely administered at low doses, and other inotropic agents and vasodilators are titrated as necessary to sustain acceptable hemodynamics. With a successful endarterectomy the cardiac output is generally high, with a low systemic vascular resistance. Temporary atrial and ventricular epicardial pacing wires are placed.

Despite the duration of extracorporeal circulation, hemostasis is readily achieved, and the administration of platelets or coagulation factors is rarely necessary. Wound closure is routine. Given the degree of preoperative volume overload, the relief of pulmonary obstruction, in addition to the previous systemic hypothermia, a vigorous diuresis is usual for the following few hours.

18.8. Results

In our most recent series involving about 1,000 patients, the mean patient age was 51.7 ± 15.4 years, with a range of 8.9–84.8 years. A similar number of men and women were referred for operation. With the exception of closure of patent foramen ovale, in 10% of cases, at least one additional cardiac procedure was performed at the time of operation. Most commonly, the adjunct procedures were coronary revascularization, aortic valve replacement, or mitral valve repair/replacement. There was no significant difference between patients undergoing pulmonary endarterectomy alone or combined with other cardiac operations with respect to cardiopulmonary bypass time, cross-clamp time, or circulatory arrest time. In general total cardiopulmonary bypass time correlates with body mass and cooling–rewarming intervals.

With this operation, a reduction in pulmonary artery pressures and pulmonary vascular resistance to normal levels and corresponding improvement in pulmonary blood flow and cardiac output are generally immediate and sustained. Improvement in the right ventricular function correlates with the decrease in the pulmonary pressures and the pulmonary vascular resistance. Generally the improvement is evident on the postoperative echocardiogram performed before discharge. This is in contrast to other conditions causing ventricular failure, and especially in disparity to the left ventricular failure caused as a result of outflow obstruction. In these patients, even when the insulting lesion or obstruction has been resolved, the ventricular dysfunction will not normalize. A good example is left ventricular failure as the result of aortic valve stenosis. After a valvular replacement, neither the LV dysfunction nor its hypertrophy will improve much. It is true that the failure will not progress, the patients will be much improved, and there may be some subtle enhancement in the LV function, but very rarely the function and size will normalize.

DropBooks

Before the operation, more than 85% of the patients were in New York Heart Association (NYHA) functional class III or IV; at the time of discharge, 80.2% were reclassified as NYHA functional class I or II. Echocardiographic studies on this patient cohort and other previous studies from our institution[18] demonstrated that with the elimination of chronic pressure overload, right ventricular geometry rapidly reverted to normal. Tricuspid valve function (as measured by tricuspid regurgitant velocity) returned to normal within a few days as a result of restoration of tricuspid annular geometry after the remodeling of the right ventricle. Tricuspid valve annuloplasty was not performed, even when severe tricuspid regurgitation was documented preoperatively.

Reperfusion edema is the single most frequent complication after pulmonary endarterectomy, occurring in up to 11% of patients. In most patients with reperfusion injury, the problem resolved with avoidance of hypercarbia, and a short period of ventilatory support and aggressive diuresis. A minority of patients with severe lung reperfusion injury required long periods of ventilatory support, and extreme cases (~1%) required veno-venous extracorporeal support for blood carbon dioxide removal and oxygenation. Neurologic complications from circulatory arrest largely have been eliminated by shorter circulatory arrest periods and the use of a direct cooling jacket placed around the head. Rates of perioperative confusion and stroke for pulmonary endarterectomy were similar to those seen with conventional open heart surgery. In our experience at UCSD, reexploration for bleeding was necessary in 3.2% of patients, and 38.8% of patients required intraoperative or postoperative blood transfusion. Despite the length of this operation, wound infection (superficial and/or deep) occurred only in 1.6% of patients.

18.9. Conclusion

It is increasingly apparent that pulmonary hypertension caused by chronic pulmonary embolism is a condition which is under-recognized, and carries a poor prognosis. Because of the obstructive nature of this disease, medical therapy remains ineffective in prolonging life and at best only transiently improves the symptoms. The only therapeutic alternative to PTE is lung transplantation. The advantages of thromboendarterectomy include a lower operative mortality and excellent long-term results without the risks associated with chronic immunosuppression and chronic allograft rejection.

Technical advances of the procedure over the last four decades, and in particular in the last 15 years, have significantly improved outcome. Attention to the surgical principles of this procedure is of paramount importance. The procedure is performed through a median sternotomy for bilateral exposure and exploration. It should be performed with the use of circulatory arrest for excellent exposure of the distal branches. The correct plane is recognized, developed, and should then be followed all the way to the distal feathered tails in each branch. With careful and meticulous intraoperative techniques as well as vigilant postoperative care, the mortality for thromboendarterectomy at our institution is now in the range of 4.5%, with sustained benefit. These results are clearly superior to those for transplantation both in the short and long term.

Although PTE is technically demanding for the surgeon, and requires careful dissection of the pulmonary artery planes and the use of circulatory arrest, excellent short- and long-term results can be achieved. It is the successive improvements in operative technique that allow pulmonary endarterectomy to be offered to patients with an acceptable mortality rate and excellent anticipation of clinical improvement. With this growing experience, we are now offering this procedure to all patients including some very high-risk candidates, as long as there is evidence of thromboembolic disease, regardless of the degree of pulmonary hypertension or right ventricular failure.

The primary problem remains that this is an under-recognized condition, and unfortunately there are still a large number of patients with CTEPH who carry other diagnoses and are mistreated as such. Increased understanding of both the prevalence of this condition and the opportunity and availability of a surgical cure should benefit more patients. Surgical removal of the thromboembolic material by means of a complete endarterectomy provides these patients an opportunity for relief from this debilitating and ultimately fatal disease.

Editor's Note:

While the bulk of the experience has been at UCSD, other selected centers worldwide have adopted this technique with reasonable results.

An alternative to circulatory arrest is antegrade cerebral perfusion at low temperatures with low-flow cardiopulmonary bypass, with acceptable visualization. One presumes that with increased use of multidetector CT scanning, we will see more of these patients being referred for further management and surgery.

18.10. Keypoints to Remember

CTEPH is a potentially treatable condition. The prognosis is best before the mean PA pressure crosses 50 mmHg and is good in patients with proximal thromboemboli.

Diagnosis of this condition requires a high index of suspicion and this is a large underdiagnosed clinical entity.

Treatment is almost always surgical. This entails complete dissection and removal of thromboemboli from both sides. Visualization of the plane between the lining of pulmonary arterial branches and thromboemboli is best under conditions of circulatory arrest. However, in selected patients and instances, antegrade cerebral perfusion with low-flow cardiopulmonary bypass may provide adequate visualization. The hallmark of success is the fall in pulmonary artery pressures immediately and gradual resolution of tricuspid regurgitation.

DropBooks

References

1. Ribeiro A, Lindmarker P, Johnsson H, et al. Pulmonary embolism: One-year follow-up with echocardiography, Doppler, and five-year survival analysis. *Circulation*. 1999;99:1325-1330.
2. Pengo V, Anthonie WA, Lensing MD, et al. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. *N Engl J Med*. 2004;350:2257-2264.
3. Becattini C, et al. Incidence of chronic thromboembolic pulmonary hypertension after a first episode of pulmonary embolism. *Chest*. 2006;130(1):172-175.
4. Dalen JE, Alpert JS. Natural history of pulmonary embolism. *Prog Cardiovasc Dis*. 1975;17:259-270.
5. Goldhaber SZ, Hennekens CH, Evans DA, et al. Factors associated with correct antemortem diagnosis of major pulmonary embolism. *Am J Med*. 1982;73:822-826.
6. Landefeld CS, Chren MM, Myers A, et al. Diagnostic yield of the autopsy in a university hospital and a community hospital. *N Engl J Med*. 1988;318:1249-1254.
7. Jamieson SW, Kapelanski DP, Sakakibara N, et al. Pulmonary endarterectomy: Experience and lesions learned in 1,500 cases. *Ann Thorac Surg*. 2003;76:1457-1464.
8. Hoeper MM, Mayer E, Simonneau G, Rubin LJ. Chronic thromboembolic pulmonary hypertension. *Circulation*. 2006;113:2011-2020.
9. Riedel M, Stanek V, Widimsky J, et al. Long-term follow-up of patients with pulmonary thromboembolism: Late prognosis and evolution of hemodynamic and respiratory data. *Chest*. 1982;81:151-158.
10. Houk VN, Hufnnagel CA, McClenathan JE, Moser KM. Chronic thrombosis obstruction of major pulmonary arteries: Report of a case successfully treated by thromboendarterectomy and review of the literature. *Am J Med*. 1963;35:269-282.
11. Jamieson SW, Kapalanski DP. Pulmonary endarterectomy. *Curr Probl Surg*. 2000;37(3):165-252.
12. Dantzker DR, Bower JS. Partial reversibility of chronic pulmonary hypertension caused by pulmonary thromboembolic disease. *Am Rev Respir Dis*. 1981;124:129-131.
13. Dash H, Ballentine N, Zelis R. Vasodilators ineffective in secondary pulmonary hypertension. *N Engl J Med*. 1980;303:1062-1063.
14. Thistlethwaite PA, Auger WR, Madani MM, et al. Pulmonary thromboendarterectomy combined with other cardiac operations: Indications, surgical approach, and outcome. *Ann Thorac Surg*. 2001;72:13-19.
15. Thistlethwaite PA, Kemp A, Du L, Madani MM, Jamieson SW. Outcomes of pulmonary endarterectomy for treatment of extreme thromboembolic pulmonary hypertension. *J Thorac Cardiovasc Surg*. 2006;131:307-313.
16. Trendelenberg F. Uber die operative behandlung der embolie derlungarterie. *Arch Klin Chir*. 1908;86:686-700.
17. Chitwood WR, Sabiston DC, Wechsler AS. Surgical treatment of unresolved pulmonary embolism. *Clin Chest Med*. 1984;5:507-536.
18. Thistlethwaite PA, Madani MM, Jamieson SW. Pulmonary thromboendarterectomy surgery. *Cardiol Clin*. 2004;22:467-478.

19
Surgical Management of Pediatric Heart Failure and Heart Failure due to Congenital Heart Disease

Emile A. Bacha

19.1. Introduction

Heart failure (HF) is a well-recognized public health problem, but in children, the scope of the problem is less well defined. Recent data from the Pediatric Cardiomyopathy Registry suggest an annual incidence of 1.1 cases of cardiomyopathy per 100,000 children.[1] The majority of children with cardiomyopathy have HF, and the mortality rate stands at 13.6% at 2 years for the dilated forms of cardiomyopathy. A further difference with adult disease is the cause of HF. Children have a genetic syndrome or diagnosis in 27% of cases, about 5% of cases are due to myocarditis, and the majority of children in end-stage HF have an underlying diagnosis of congenital heart disease.[2,3] HF in children may develop from myocyte dysfunction or on the basis of congenital disorders resulting in volume or pressure overload. Both the latter conditions are typically addressed surgically or via interventional techniques. Management guidelines for adult HF have been extensively documented and published. Only recently have practice guidelines for management of HF in children been published.[4] Even the use of the term HF in children can be ambiguous because it often includes children with uncorrected structural lesions resulting in left to right shunting with usually preserved systolic function.

19.2. Surgical Management of Heart Failure in the Systemic Right Ventricle

This group of patients essentially includes two diagnostic groups:

1. Patients with D-transposition of the great arteries (D-TGA) who were treated mostly before the 1980s with an atrial switch procedure (Senning or Mustard repair).
2. Patients born with congenitally corrected transposition of the great arteries (CCTGA). This is a rare anomaly that comprises less than 1% of all patients with congenital heart disease. Patients with CCTGA have their ventricles "inverted," that is, right atrial systemic venous blood goes into the left ventricle and then the pulmonary artery (PA); the left atrial pulmonary venous blood empties into the right ventricle and then the aorta.

19.2.1. Patients with D-Transposition of the Great Arteries

D-TGA is the fifth or sixth most common diagnosis in congenital heart disease. Before the 1980s, patients with D-TGA were being treated routinely with atrial switches and achieved survival rates of >90%. Therefore, there are a substantial number of survivors who are now adults and will likely

develop various degrees of systemic ventricular dysfunction. Right ventricular (RV) performance at rest may be normal,[5] but these patients' exercise ability is often limited because of chronotropic incompetence (likely due to atrial baffle suture lines) and limited stroke volume reserve.[6,7] Further potential etiologies for late systemic RV dysfunction after atrial switch include different mechanics and fiber arrangements of the RV compared to the LV, a definite incidence of baffle leaks or obstruction resulting in suboptimal hemodynamics due to atrial level shunting, the ability of the tricuspid valve to function in the systemic circulation with late onset of tricuspid insufficiency, and myocardial fibrosis secondary to prolonged hypoxemia during infancy (while waiting for surgery) or poor (sometimes none except for hypothermia) myocardial protection during repair.[8] Chronic subendocardial ischemia has been described using single photon emission computed tomography.[9]

Medical management is essentially based on that of adult patients with systemic LV failure. Before embarking on surgical therapy, it is essential to evaluate adult patients completely and thoroughly by all available means, including angiograms. Often, structural anomalies that are present can be diagnosed and repaired. The most commonly found anomaly late after atrial switch is baffle leaks that can lead to significant left-to-right shunting and HF. These can often be occluded in the catheterization laboratory using devices. Baffle stenosis can result in venous occlusion of either the superior vena cava (SVC) or the inferior vena cava (IVC). Surgery is often needed as interventional approaches often fail to close baffle leaks or dilate (or stent) stenoses in the atrial baffles. Structural valve problems can also mimic symptoms of HF and should be aggressively thought out. In particular, the systemic tricuspid valve is not designed to withstand systemic pressures and thus may require repair or replacement. The principles of repair or replacement of the systemic tricuspid valve are essentially the same as those for mitral valve surgery, except that it will be in an anterior location and thus more easily accessible to the surgeon.

For patients with no structural problems and systemic RV failure, there are two options: a heart transplant or an atrial baffle takedown accompanied by an arterial switch procedure. The former follows the usual principles of heart transplantation in adults whereby all connections will be in their usual anatomic location (the great vessels may be less rotated and more in an anterior–posterior relationship, with the aorta anterior to the PA). The atrial baffle takedown and arterial switch procedure have been done in selected centers only. The central problem is to retrain or recondition the LV (usually with sequential PA banding with or without an additional aortopulmonary shunt) in order for it to function in the systemic circulation.[10] Roughly one-third of patients respond unfavorably to PA banding, with a mortality of 14% for this procedure.[10] In particular, the response to morphologically left ventricular reconditioning past adolescence has been inconsistent, and patients older than 12 years are likely to be better served with heart transplantation. However, in selected (mostly young) patients, atrial baffle takedown and arterial switch procedure is a viable alternative to cardiac transplantation with good long-term results.

19.2.2. Patients with CCTGA

Unlike late atrial switch survivors, the clinical course of patients with CCTGA is often determined by associated structural defects such as ventricular septal defects, tricuspid valve (systemic atrio-ventricular valve) prolapse and regurgitation, pulmonary stenosis, or by electrophysiologic anomalies such as atrioventricular block. Patients with CCTGA (mainly those who lack any associated anomalies) can function well into adulthood. However, the majority will have systemic RV dysfunction and HF with advancing age. By 45 years of age, 25% of patients without and 67% of patients with associated lesions have HF.[11] This is why some have advocated early performance of a double-switch operation.[12] The double-switch operation can be performed with excellent hospital and long-term survival preferably at a young age. However, the theoretical advantages of this procedure, which enables the morphologic left ventricle and mitral valve to support a systemic pressure load, must be established by careful follow-up of these patients. In older patients presenting in HF, the surgical management is similar to that of patients with atrial switch operations. In the presence of structural anomalies, surgery should be strongly considered. When RV dysfunction is associated with tricuspid

DropBooks

valve insufficiency, and particularly when there is associated structural valve disease, surgery in the form of either repair or replacement should be performed. A recent retrospective study of 123 patients showed that right HF and need for tricuspid valve surgery were significant risk factors for death at any time.[13] Patients with advanced RV dysfunction refractory to medical management should be considered for heart transplantation.

19.3. Surgical Management of Chronic Heart Failure in the Univentricular Circulation

The majority of patients born with single ventricles undergo surgical palliation early on in the form of a stage I Norwood procedure, a PA band, or an aortopulmonary shunt first, followed by a bidirectional cavopulmonary anastomosis and ultimately the Fontan procedure (total cavopulmonary connection). Early palliation with complete mixing of systemic and pulmonary venous blood (as in the Norwood, aortopulmonary shunt, or PA band procedures) requires that ventricular output must be maintained at a level that is —two to three times normal.[14,15] After final palliation (Fontan operation), the durability of the systemic ventricle (in particular right ventricle) is questionable.[16,17]

Manifestations of HF in single-ventricle patients can be varied and are often related to the high systemic venous pressures, which by necessity is higher than the pulmonary pressure (passive flow into the lungs). In addition, their limited exercise capacity may or may not be related to ventricular dysfunction, as systemic or pulmonary venous obstruction, valve regurgitation, or arrhythmias are also associated with worse outcomes. Survival rates after a “perfect” Fontan operation have been reported to be between 70% and 90% at 5 years and 60% and 80% at 10 years.[3,18] In general, invasive hemodynamic evaluation is needed to document myocardial dysfunction and rule out other potentially treatable factors. If unresponsive to medical, surgical, and catheter-based intervention, cardiac transplantation is the only therapeutic recourse available. Patients with single-ventricle physiology now comprise 70–80% of patients transplanted for congenital heart disease.[3] With increased survival rates after stage I palliation, that proportion is likely to increase. A recent retrospective study of a large patient cohort[3] showed that the majority (57%) of patients underwent heart transplant for HF due to systolic ventricular dysfunction. However, 43% of transplanted patients had preserved systolic function with presence of significant exercise intolerance due to failed Fontan circulation (signs and symptoms of poor cardiac output in the absence of ventricular dysfunction).

Figure 19.1 shows the steps involved in the first step of palliation, the cavo-pulmonary connection also known as the Glenn shunt.

Heart transplantation in patients with single-ventricle physiology poses unique challenges, the most common of which are listed below:

1. They have usually undergone multiple surgical procedures with resulting vascular adhesions from microscopic aortopulmonary or veno-venous collaterals as well as sternal deformities.
2. They therefore often require inguinal access for establishment of cardiopulmonary bypass. This may be complicated by vessel occlusions in the lower body due to the multiple

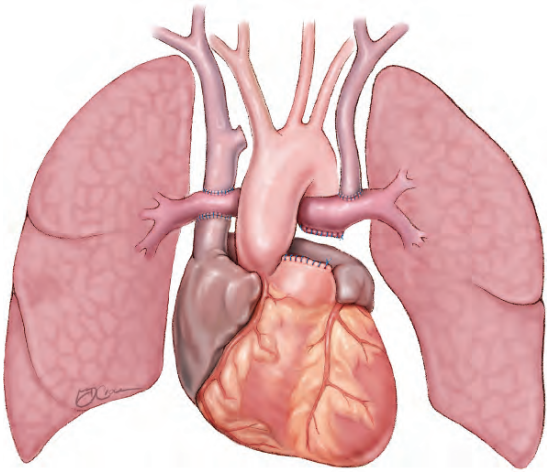


FIGURE 19.1. The completed Glenn Cavo-pulmonary connection. This shows the oversewn main pulmonary artery (PA), the superior vena cava (SVC) sutured to the main PA above and below, and the left SVC sutured to the left branch PA.

catheterizations they have typically undergone. Lower body vascular studies are a must prior to transplant.
3. More than 90% of patients[3] will require reconstructive surgery such as PA reconstruction or rerouting of pulmonary venous pathways with concomitant prolongation of ischemic and cardiopulmonary bypass times.
4. Pulmonary arterio-venous malformations, which most single-ventricle patients have acquired to various degrees, can be a major obstacle postoperatively, resulting in significant left-to-right shunting and high-output congestive HF. These patients may require urgent coil occlusion postoperatively.
5. They have had years of long-standing elevated systemic venous pressures with resultant end-organ damage such as liver fibrosis or kidney damage.
6. They are often chronically debilitated with severely limited functional capacity.
7. Protein-losing enteropathy is a poorly understood long-term complication of single-ventricle physiology and can be sometimes effectively treated with cardiac transplantation.[3,19] However, it is also clearly a risk factor for death after transplant.[3]

For the reasons mentioned above, the postoperative course is usually more complicated than with non–single-ventricle recipients. Infection is a common problem, occurring in as much as 22% of recipients.[3] This compares to a 7–30% incidence of infection in patients transplanted for all causes.[20] Overall Kaplan–Meier survival curves for transplantation in single-ventricle patients show survival rates of 72% at 1 year and 62% at 10 years in the most recent large study.[3] The registry of the International Society for Heart and Lung Transplantation has reported that congenital heart disease of any kind is a significant risk factor for 1-year survival.[21] There currently exists an increasing number of long-term survivors after the Fontan procedure. Cardiac transplantation remains the standard option for those with failed single-ventricle physiology. However, more efforts should be expanded toward patient selection and timing of transplantation in an effort to improve outcomes.

19.4. Acute Heart Failure After Surgery for Congenital Heart Disease

Mechanical circulatory support has become a crucial element of postoperative management of children after surgery for congenital heart disease. The largest experience in the pediatric population is with extracorporeal membrane oxygenation (ECMO),[22] primarily because size limitations have precluded extensive use of other modalities. However, smaller ventricular assist devices are being developed primarily in Europe, and have even been applied to neonates.[23] There currently is no FDA-approved pediatric ventricular assist device in the United States. Adolescents and children weighing more than 45 kg can often be supported by the currently available adult-size ventricular assist devices. The choice of modality in a given patient will depend on the age and size of the patient, the specific pathophysiology, on the availability of support devices, and on physician expertise.

Traditional indications have included low cardiac output unresponsive to pharmacologic support or resuscitation after cardiac arrest. With improved survival rates after mechanical support, these indications have recently evolved to include earlier institution of mechanical support in children with increasing inotropic support and end-organ malperfusion or neonates after stage I palliation.[24] Mechanical assist can be used to recover patients after surgery, with cardiac remodeling occurring during support. Incomplete repairs or remaining residual hemodynamic lesions should be aggressively thought out by echocardiography and angiography and repaired if present. Similarly, patients who fail to wean from cardiopulmonary bypass can effectively be transitioned to mechanical support after residual lesions have been excluded. Overall, the outcomes in the group of patients placed on mechanical support during the postoperative period is less satisfactory than for other indications of mechanical support such as myocarditis or intractable arrhythmias.[22] A recent study looking at a 10-year experience in 96 patients revealed a 40% survival to hospital discharge.[25] Furthermore, the use of mechanical support in single-ventricle

DropBooks

patients has been associated with poorer outcomes, although recent studies show some improvement.[24] When cardiac recovery is not expected, mechanical support can be used as a bridge to transplant.[26] Long-term outcomes among those undergoing heart transplantation after support with ECMO are comparable with those of patients not receiving ECMO.[26] Extracorporeal membrane oxygenation can also be a useful posttransplant support device. Cannulation for ECMO is typically done via the sternotomy in the case of postoperative patients, and via the right-sided neck vessels for patients who do not have a recent sternotomy.

Figure 19.2 shows the Glenn shunt being taken down to allow implant of heart transplant and Figure 19.3 shows the new heart with the circulation connected the normal way.

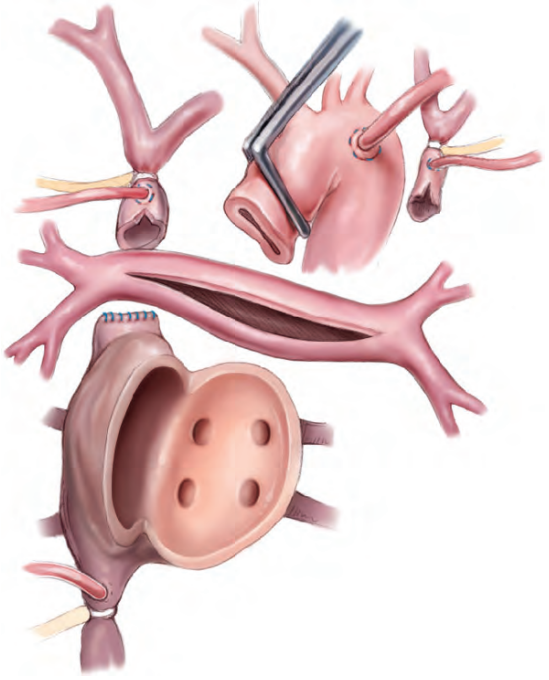


FIGURE 19.2. The aorta cross clamped and the Glenn connected being taken down; the superior vena cava (SVC) transected and opened just about the right atrium; a longitudinal incision in the main pulmonary artery (PA); a divided left SVC; and an opened atrium.

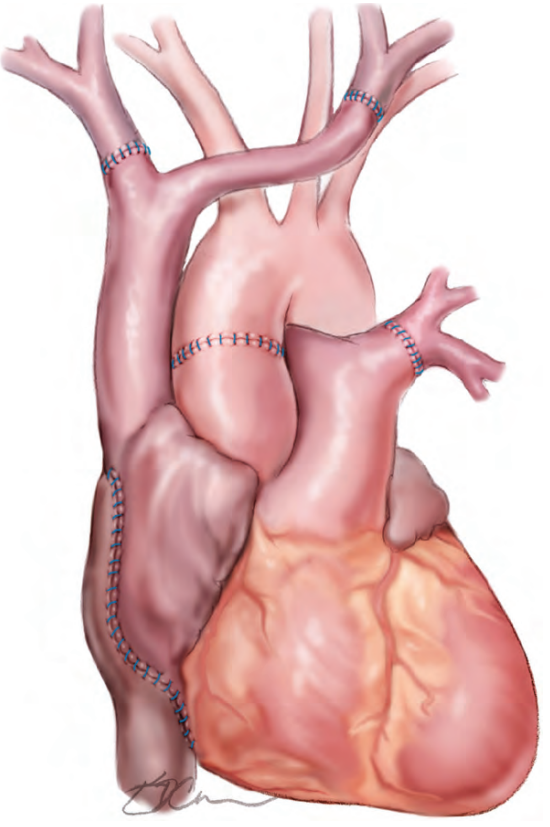


FIGURE 19.3. The completed heart transplant after these connections have been hooked up to the new heart.

Key Points to Remember

- Heart failure in children is an important problem, the scope of which is less well defined than in the adult population. This is associated with a high mortality and morbidity.
- More than a quarter of the pediatric heart failure patients have a genetic basis.
- A significant number of children with complex congenital anomalies are born or end up with single ventricle physiology which makes management complicated.
- Options for mechanical assistance of end-stage heart failure are very limited in children.
- Transplantation in children is severely limited by donor organ shortage.

References

1. Lipshultz SE, Sleeper LA, Towbin JA, et al. The incidence of pediatric cardiomyopathy in two regions of the United States. *N Engl J Med*. 2003;348:1647-1655.
2. Boucek MM, Edwards LB, Keck BM, et al. The registry of the International Society for Heart and Lung transplantation: Sixth official pediatric report-2003. *J Heart Lung Transplant*. 2003;22:636-652.
3. Jayakumar KA, Addonizio LJ, Kichuk-Chrisant MR, et al. Cardiac transplantation after the Fontan or Glenn procedure. *J Am Coll Cardiol*. 2004;44:2065-2072.
4. Rosenthal D, Chrisant MRK, Edens E, et al. International Society for Heart and Lung Transplantation: Practice guidelines for management of heart failure in children. *J Heart Lung Transplant*. 2004;23:1313-1333.
5. Redington AN, Rigby ML, Shinebourne EA, Oldershaw PJ. Changes in the pressure/volume relation of the right ventricle when its loading conditions are modified. *Br Heart J*. 1990;63:45-49.
6. Hagler DJ, Ritter DG, Mair DD, et al. Right and left ventricular function after the Mustard procedure in transposition of the great arteries. *Am J Cardiol*. 1979;44:276-283.
7. Reybrouck T, Gewillig M, Dumoulin M, van der hauwaert LG. Cardiorespiratory exercise performance after Senning operation for transposition of the great arteries. *Br Heart J*. 1993;70:175-179.
8. Fogel MA, Weinberg PM, Fellows KE, Hoffman EA. A study in ventricular-ventricular interaction. Single right ventricles compared with systemic right ventricles in a dual chamber circulation. *Circulation*. 1995;92:219-230.
9. Millane T, Bernard EJ, Jaeggi E, et al. Role of ischemia and infarction in late right ventricular dysfunction after atrial repair of transposition of the great arteries. *J Am Coll Cardiol*. 2000;35:1661-1668.
10. Poirier NC, Yu JH, Brizard CP, Mee RB. Long-term results of left ventricular reconditioning and anatomic correction for systemic right ventricular dysfunction after atrial switch procedures. *J Thorac Cardiovasc Surg*. 2004;127:975-981.
11. Graham TP Jr, Bernard YD, Mellen BG, et al. Long-term outcome in congenitally corrected transposition of the great arteries: A multi-institutional study. *J Am Coll Cardiol*. 2000;36:255-261.
12. Duncan BW, Mee RB, Mesia CI, et al. Results of the double switch operation for congenitally corrected transposition of the great arteries. *Eur J Cardiothorac Surg*. 2003;24(1):11-19.
13. Hraska V, Duncan BW, Mayer JE Jr, et al. Long-term outcome of surgically treated patients with corrected transposition of the great arteries. *J Thor Cardiovasc Surg*. 2005;129:182-191.
14. Sluysmans T, Sanders SP, van der Velde M, et al. Natural history and patterns of recovery of contractile function in single left ventricle after Fontan operation. *Circulation*. 1992;86:1753-1761.
15. Tanoue Y, Sese A, Ueno Y, Joh K, Hijii T. Bidirectional Glenn Procedure improves the mechanical efficiencyt of a total cavopulmonary connection in high-risk fontan candidates. *Circulation*. 2001;103:2176-2180.
16. Berman NB, Kimball TR. Systemic ventricular size and performance before and after the bidirectional cavopulmonary anastomosis. *J Pediatr*. 1993;122:S63-S67.
17 Mahle WT, Coon PD, Wernovsky G, Rychik J. Quantitative echocardiographic assessment of the performance of the functionally single right ventricle after the Fontan operation. *Cardiol Young*. 2001;11:399-406.
18. Lamour JM, Addonizio LJ, Galantowicz ME, et al. Outcome after orthotopic cardiac transplantation in adults with congenital heart disease. *Circulation*. 1999;100(suppl):II200-II205.
19. Mertens L, Hagler DJ, Sauer U, et al. Protein-losing enteropathy after the Fontan operation: an international multicenter study. *J Thorac Cardiovasc Surg*. 1998;115:1063-1073.
20. Doelling NR, Kanter KR, Sullivan KM, et al. Medium term results of pediatric patients undergoing orthotopic heart transplantation. *J Heart Lung Transplant*. 1997;16:1225-1230.
21. Boucek MM, Edwards LB, Keck BM, et al. The registry of the International Society for Heart and Lung transplantation: Fifth official pediatric report-2001 to 2002. *J Heart Lung Transplant*. 2002;21:827-840.
22. Duncan BW. Mechanical circulatory support for infants and children with cardiac disease. *Ann Thorac Surg*. 2002;73:1670-1677.
23. Sidiropoulos A, Hotz H, Konertz W. Pediatric circulatory support. *J Heart Lung Transplant*. 1998;17:1172-1176.
24. Shen I, Ungerleider RM. Routine use of mechanical ventricular assist following the Norwood procedure. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2004;7:16-21.
25. Ibrahim AE, Duncan BW, Blume ED, Jonas RA. Long-term follow-up of pediatric cardiac patients requiring mechanical circulatory support. *Ann Thorac Surg*. Jan 2000;69(1):186-192.
26. Kirshbom PM, Bridges ND, Myung RJ, Gaynor JW, Clark BJ, Spray TL. Use of extracorporeal membrane oxygenation in pediatric thoracic organ transplantation. *J Thorac Cardiovasc Surg*. 2002;123(1):130-136.

DrJonBooks

20
Anesthetic Management and Hemodynamic Management

Mark A. Chaney

20.1. Introduction

Medical management of patients with heart failure is certainly challenging. Perioperative anesthetic management of these oftentimes extremely sick individuals is even more challenging for a wide variety of reasons (essentially all anesthetic techniques compromise the cardiovascular system, patients are undergoing major invasive surgery, detrimental physiologic effects associated with cardiopulmonary bypass, etc.). In order to ensure acceptable postoperative outcome, a true team approach is required by the surgeon, anesthesiologist, perfusionist, and nursing staff. Adequate communication is required by all to identify and attain perioperative goals. The anesthesiologist's job is to choose and safely administer an appropriate anesthetic technique for each particular patient undergoing his or her specific surgery. Most times, no specific drug or technique is truly indicated. As we will see, identified goals (analgesia, amnesia, muscle relaxation) can be safely attained in many ways. One of the most challenging tasks confronting the anesthesiologist when managing these patients is that of maintaining perioperative hemodynamic stability. The key to successfully managing this problem is correctly identifying the cause of hemodynamic instability (preload, myocardial contractility, afterload) via a wide variety of monitoring techniques (electrocardiography, pulmonary artery catheter, transesophageal echocardiography, etc.). Once again, as we will see, identified goals (optimize preload, optimize myocardial contractility, optimize afterload) can be safely attained in many ways.

The successful perioperative anesthetic management of patients with heart failure is complex and challenging. Anesthesiologists managing these patients need to have extensive knowledge regarding cardiovascular physiology and pharmacology, physiologic effects of anesthetic drugs and techniques on the cardiovascular system, and rational assessment/pharmacologic treatment of hemodynamic instability. In the current era, all such anesthesiologists managing these extremely sick individuals should possess appropriate skills regarding the use of transesophageal echocardiography. Identified perioperative goals may be attained safely in many ways. Thus, there is much "art" (which requires extensive clinical experience) to the successful perioperative anesthetic management of patients with heart failure.

20.2. Anesthetic Management

20.2.1. Preoperative Assessment

The goals of preoperative assessment include reducing surgical morbidity, increasing quality and decreasing cost of perioperative care, and allowing the patient to return to desirable functioning as quickly as possible. Traditionally, the anesthesiologist will meet with the patient to review medical and surgical history, order appropriate laboratory tests, obtain informed consent, educate the patient regarding all aspects of perioperative care, and answer questions the patient may have.

Table 20.1 lists items reviewed by the anesthesiologist during preoperative assessment. Numerous

Table 20.1. Preoperative assessment.

Age/gender/race/height/weight
Proposed surgery
Past medical history
Past surgical history
Allergies
Current medications
Vital signs
Physical examination
Laboratory tests
Additional tests

Table 20.2. Agents commonly used during anesthesia.

Intravenous opioids
Morphine, fentanyl, sufentanil
Intravenous benzodiazepines
Diazepam, midazolam
Inhaled anesthetics
Isoflurane, desflurane, sevoflurane
Intravenous alpha-2 receptor agonists
Dexmedetomidine
Intravenous muscle relaxants
Pancuronium, vecuronium, rocuronium

factors profoundly influence perioperative anesthetic management. For instance, the presence of renal failure and/or hepatic failure dictates which specific anesthetic medications may or may not be administered. Specifically regarding patients with heart failure, knowledge of current cardiac medications (beta-adrenergic blockers, diuretics, digitalis, etc.) is required prior to planning technique of anesthesia. Additionally, certain preoperative tests (echocardiography, cardiac catheterization, etc.) give the anesthesiologists valuable information regarding left ventricular function and valvular function; again, knowledge required prior to planning technique of anesthesia.

Patients with heart failure undergo a wide variety of surgical procedures. Thus, it is important for all perioperative caregivers (surgeon, anesthesiologist, perfusionist, and nursing staff) to "be on the same page" regarding the planned surgical procedure (coronary artery bypass grafting, valve repair or replacement, ventricular reconstruction, etc.). Additionally, it should be determined whether or not cardiopulmonary bypass will be utilized. Numerous surgical procedures are now being attempted without assist of cardiopulmonary bypass (off-pump).

If cardiopulmonary bypass is to be utilized, it should be clear to all what specific technique will be used (normothermic, hypothermic, beating heart, arrested heart, etc.). The planned surgical procedure and use/nonuse/technique of cardiopulmonary bypass (decisions arrived at oftentimes only after intraoperative transesophageal echocardiographic evaluation) profoundly influence technique of anesthesia.

20.2.2. Goals of Anesthetic Management

The major goals of anesthesia include analgesia (pain relief), amnesia (lack of recall), hemodynamic stability, and perhaps muscle relaxation (paralysis). Table 20.2 presents the variety of most common ways the anesthesiologist may safely attain these goals (methods of attaining hemodynamic stability will be addressed later). Most commonly, a combination of intravenous opioid (analgesia), intravenous benzodiazepine (amnesia), and inhalational anesthetic (analgesia and amnesia) is used. In the current era of "fast-tracking," specific drugs and amounts are chosen for specific anesthetic goals in each individual patient in order to allow the patient to awaken from anesthesia in the immediate postoperative period. Thus, short-acting drugs (fentanyl, midazolam) and/or inhalational anesthetics are favored.

20.2.3. Monitored Anesthesia Care

The term monitored anesthesia care generally implies simple intravenous sedation. Most commonly, a combination of intravenous opioid and intravenous benzodiazepine is administered to a spontaneously breathing patient. Because amounts of opioid and benzodiazepine must be carefully kept to an appropriate minimum (both drug classes promote respiratory depression), only certain minimally invasive surgeries may be performed in patients with heart failure under monitored anesthesia care (pacemakers, etc.).

DropBooks

20.2.4. Regional Anesthesia

The term regional anesthesia generally implies the use of a wide variety of peripheral nerve blocks (parasternal block, intercostal nerve block, etc.), intrathecal techniques, and/or epidural techniques.[1] While general anesthesia may be supplemented with regional anesthetic techniques, the traditional use of the term regional anesthesia usually implies the use of regional anesthetic techniques and intravenous sedation in a spontaneously breathing patient. Thus, amounts of intravenous opioid and benzodiazepine must be carefully kept to an appropriate minimum, limiting the scope of surgeries that may be performed in patients with heart failure under regional anesthesia.

Use of regional anesthetic techniques in patients undergoing cardiac surgery, while seemingly increasing in popularity, remains extremely controversial, prompting numerous editorials by recognized experts in the field of cardiac anesthesia. One of the main reasons such controversy exists (and likely will continue for some time) is that the numerous clinical investigations regarding this topic are suboptimally designed and utilize a wide array of disparate techniques preventing clinically useful conclusions all can agree on.[2–5]

20.2.5. General Anesthesia

The term general anesthesia usually implies the use of moderate to large doses of intravenous agents and/or inhalational agents (with or without intravenous muscle relaxants) along with endotracheal intubation and mechanical ventilation. The vast majority of cardiac surgeries performed in patients (with or without heart failure) are performed under general endotracheal anesthesia. The total control over the respiratory system via mechanical ventilation allows the anesthesiologist to administer large amounts of intravenous anesthetics and/or inhalational anesthetics to the patient, permitting invasive cardiac surgery to occur. General anesthesia is sometimes supplemented with regional anesthetic techniques.

20.2.6. Premedication

The goals of premedication include decreased patient anxiety, production of amnesia, and minimization of pain associated with vascular cannulation in the preanesthetic period without producing ventilation or cardiac depression. These goals are most commonly met by administering small and appropriate amounts of intravenous opioids for analgesia and intravenous benzodiazepines for amnesia. Additionally, most anesthesiologists have patients take their routine cardiovascular medications (beta-adrenergic blockers, etc.) the morning of surgery (with small sips of water) in hopes of promoting perioperative hemodynamic stability.

20.2.7. Monitoring

Numerous physiologic parameters are monitored in patients undergoing cardiac surgery (Table 20.3). Arterial blood pressure may be monitored noninvasively or invasively. Cardiac rate and rhythm is assessed via electrocardiography. Cardiac function (preload, myocardial contractility, etc.) is most commonly monitored via the pulmonary artery catheter and/or transesophageal echocardiography, and will be discussed in greater detail later in this chapter. Pulmonary function is assessed in a wide variety of ways, including assessment of pulmonary compliance and interpretation of arterial blood gas tensions (oxygen, carbon dioxide). Urine output is closely monitored in all patients undergoing cardiac surgery, especially so in patients with preoperative renal dysfunction. Maintenance of normothermia in patients is extremely important (and sometimes difficult), especially in cardiac surgeries without assist of cardiopulmonary bypass. Numerous arterial blood samples are obtained perioperatively in order to monitor pulmonary function, a wide variety of serum electrolytes (potassium, magnesium, etc.), glucose levels, and hemoglobin levels. Frequent assessment of coagulation is important as

TABLE 20.3. Monitored physiologic parameters.

Arterial blood pressure
Cardiac rate and rhythm
Cardiac function
Pulmonary function
Renal function
Body temperature
Blood gas analysis
Coagulation analysis
Cerebral function

well, because essentially all patients undergoing cardiac surgery will be subjected to at least some degree of anticoagulation (and possibly reversal of anticoagulation). Cerebral function monitoring is somewhat controversial. Neurologic insult (via microemboli and/or macroemboli) continues to haunt cardiac surgery. Although numerous investigators have valiantly tried, we are still without a monitor that reliably and effectively predicts neither intraoperative recall nor development of postoperative neurologic insult (stroke or diffuse neuropsychological dysfunction).

20.2.8. Induction of General Anesthesia

Prior to induction of general anesthesia in patients scheduled for cardiac surgery, a wide variety of items need to be prepared and checked out. The anesthesia machine needs to be checked out and airway materials (laryngoscope) prepared. Appropriate medications (anesthetic drugs, potent cardiovascular drugs) need to be prepared as well. Currently, peripheral venous access is obtained and intravenous premedication administered. Most anesthesiologists insert invasive arterial catheters (usually radial artery) prior to induction of general anesthesia. Safe induction of general anesthesia in patients with heart failure can be accomplished in a wide variety of ways. Any one of a combination of anesthetic drugs can be selected on the basis of both their anesthetic properties and their hemodynamic effects. However, one must realize that essentially all intravenous and inhalational anesthetics can initiate profound (dose-related) cardiorespiratory depression. Additionally, the anesthesiologist should thoroughly understand the patient's underlying cardiac status (left ventricular function, extent of valvular disease, etc.) prior to induction of general anesthesia because specific choices of anesthetic drugs may be determined by specific physiologic goals in individual patients (e.g., avoidance of arterial vasodilation in a patient with aortic stenosis). Most commonly, a combination of intravenous opioid (analgesia), intravenous benzodiazepine (amnesia), and inhalational anesthetic (analgesia and amnesia) is used. Following induction of general anesthesia, the trachea is intubated with a cuffed endotracheal tube (following administration of an intravenous muscle relaxant). The choice of a particular muscle relaxant is based upon pharmacokinetics (speed of onset, half-life, etc.) and autonomic and hemodynamic side effects. In most patients, tracheal intubation is accomplished via direct laryngoscopy. However, in patients with altered airway anatomy, tracheal intubation must be accomplished in another manner (awake fiberoptic, asleep fiberoptic, etc.). Once the airway is secured, mechanical ventilation is appropriately initiated.

20.2.9. Maintenance of General Anesthesia

Maintenance of general anesthesia involves continued administration of intravenous anesthetics and/or inhalational anesthetics to achieve the goals of analgesia and amnesia (and possibly muscle relaxation). While muscle relaxation during cardiac surgery is not required, it is often achieved for a wide variety of reasons (facilitate endotracheal intubation, limit oxygen consumption, prevent shivering, and prevent unexpected movement during critical periods of the operation). The drawback of continuous muscular paralysis is its interference with somatic signs (movement) of light anesthesia. If cardiopulmonary bypass is used, maintenance of general anesthesia is attained via continued administration of intravenous anesthetics and/or inhalational anesthetics.

20.2.10. Emergence from General Anesthesia

With the focus on reducing costs by shortening the length of stay in the intensive care unit, the anesthesiologist in encouraged to design an anesthetic plan that not only fulfills the requirements of general anesthesia (analgesia, amnesia, muscle relaxation, hemodynamic stability, etc.) during intense noxious stimulation intraoperatively but also allows an appropriately rapid recovery of consciousness and spontaneous ventilation postoperatively. In the uncomplicated case, the goal is to allow tracheal extubation very soon after the patient's condition is stabilized in the intensive care unit, usually within 2–4 h postoperatively. Hence, there is continuing effort to develop rapid-onset, short-acting anesthetics, opioids, benzodiazepines, and muscle relaxants that allow efficient titration of dose (or infusion

DropBooks

rate) according to the individual patient's needs both intraoperatively and postoperatively.

20.3. Hemodynamic Management

Potential therapeutic interventions in managing patients with hypotension and/or decreased cardiac output include manipulation of heart rate or rhythm, optimizing preload, optimizing myocardial contractility, and/or optimizing systemic vascular resistance.[6,7] When managing patients with hypotension and/or decreased cardiac output, the initial important task for the clinician is to appropriately assess the hemodynamic instability to determine the etiologic roles that heart rate/rhythm, preload, myocardial contractility, and/or systemic vascular resistance contribute to the hemodynamic instability. Once the cause(s) of hemodynamic instability is identified, the physiologic goal(s) is identified and appropriate specific therapy is initiated. Such decisions are clinically important. Appropriate clinical interventions can prove lifesaving. Conversely, inappropriate clinical interventions can prove deadly. For example, administering a vasoconstrictor to a patient who has hypotension/decreased cardiac output from left ventricular failure will most certainly precipitate clinical deterioration. This patient requires agents that increase myocardial contractility and/or initiate afterload reduction (not vasoconstrictors). Section 20.3.1 will focus on how clinicians should appropriately assess hemodynamic instability, choose the physiologic goal(s), initiate appropriate specific therapy, and assess the outcome of the chosen therapy.[8,9]

20.3.1. Hemodynamic Instability Assessment

Numerous clinical variables must be contemplated during assessment of hemodynamic instability (Table 20.4). Determination of blood pressure and evaluation of heart rate and rhythm obviously play an important role in initial early assessment of hemodynamic instability. Level of hypotension (mild, moderate, severe) determines the time frame in which the clinician must operate. In certain patients, manipulation of heart rate and/or heart rhythm may restore hemodynamic stability. While the physical examination may be of great value in diagnosing gross or acute pathology (pneumothorax, hemothorax, acute valvular insufficiency), it is of limited value in diagnosing and managing ventricular failure. While level of mental status and amount of urine output may be beneficial in certain patients, classic clinical indicators of decreased cardiac output (oliguria, metabolic acidosis) may not always be reliable. Thus, in essentially all patients with clinically significant hemodynamic instability that requires more than routine therapy, more information will be required then is routinely obtained in order to appropriately assess the hemodynamic instability. Such information is most commonly obtained via assessment of central venous pressure, insertion of a pulmonary artery catheter, and/or some form of echocardiography. Each of these three methods has unique advantages and disadvantages.

Table 20.4. Hemodynamic instability assessment.

Blood pressure/heart rate
Electrocardiogram
Mental status/urine output
Arterial/venous blood analysis
Central venous pressure
Pulmonary artery catheter
Echocardiography

The routine use of a pulmonary artery catheter in all patients with hemodynamic instability has progressively been replaced by a more selective approach. In general, a central venous pressure catheter alone may be used for monitoring in patients with preserved left ventricular function (ejection fraction > 40%) and no severe valvular pathology. If the patient continues to clinically deteriorate (progressive hypotension, unexplained oliguria, and/or acidosis), then a pulmonary artery catheter may be inserted to gather additional information, such as right ventricular pressure, pulmonary artery pressure, and pulmonary artery occlusive pressure. Derived variables, such as cardiac output/cardiac index, pulmonary vascular resistance, and systemic vascular resistance, may also then be obtained. Special purpose pulmonary artery catheters for continuous cardiac output measurements, continuous mixed venous oximetry measurements, pacing ability, and/or right ventricular ejection fraction are also available.

Table 20.5. Comparison of pulmonary artery catheter data and echocardiography data.

Determinant	Pulmonary artery catheter data	Echocardiography data
Preload	CVP, PAOP	Direct
Afterload	SVR	All stress
Systolic function	SV, CO	FAC, EF, SV, CO, ESPVR
Diastolic function	CVP, PAOP	Filling profiles
Ischemia	Insensitive	Sensitive
Valvular function	Indirect	Direct
Aneurysm/dissection	Not useful	Extremely useful
Effusion/tamponade	Indirect	Direct
Intracardiac catheters	Not useful	Extremely useful

CVP central venous pressure, *PAOP* pulmonary artery occlusion pressure, *SVR* systemic vascular resistance, *SV* stroke volume, *CO* cardiac output, *FAC* fractional area change, *ESPVR* end-systolic pressure–volume relation

The introduction of the flow-directed pulmonary artery catheter in the 1970s represented, at the time, a major advance in the monitoring of hemodynamically unstable patients. A very large amount of information (intracardiac pressures, derived hemodynamic and pulmonary parameters) can be gathered. However, one must keep in mind that clinical data obtained from a pulmonary artery catheter may be erroneous and/or misleading.[10,11] Some recent clinical investigations have indicated that information obtained from pulmonary artery catheters may in fact lead clinicians to initiate inappropriate therapy, which may increase morbidity and mortality. Such clinical investigations have stirred controversy regarding proper clinical utilization of (and interpretation of data from) the pulmonary artery catheter. Some investigators/editors have even suggested that use of the pulmonary artery catheter should be abandoned.

Probably the major reason for the "demise" of the pulmonary artery catheter has been the emergence of echocardiography (specifically transesophageal echocardiography) over the past two decades. It is now clear that information obtained from echocardiography is far superior (in quality and quantity) to that obtained from the pulmonary artery catheter. Furthermore, information from echocardiography has helped prove that much of the information obtained from the pulmonary artery catheter may be erroneous and/or misleading. Specifically, echocardiography provides definitive clinical data regarding preload, myocardial contractility, and systemic vascular resistance whereas the pulmonary artery catheter can only provide surrogates of these important variables. Furthermore, echocardiography can provide additional useful clinical data that the pulmonary artery catheter cannot, such as information regarding diastolic function, myocardial ischemia, valvular function, potential aneurysm/dissection, potential effusion/tamponade, and the presence/position of intracardiac catheters (Table 20.5). The American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography deemed that unexplained hemodynamic disturbances not responsive to conventional therapy is a Class I indication for use of transesophageal echocardiography ("frequently useful in improving clinical outcome").[12]

DropBooks

20.3.2. Physiologic Goals of Therapy

By utilizing a clinically appropriate physical examination, invasive monitoring (central venous pressure, pulmonary artery catheter), and/or echocardiography, one can determine the physiologic goal(s) of therapy. Once assured that heart rate and rhythm are optimized, the clinician must then choose the appropriate mixture of optimizing intravascular volume, optimizing myocardial contractility, and/or optimizing systemic vascular resistance (Table 20.6). The relative importance of each (preload, myocardial contractility, afterload) will vary in each individual patient and clinical scenario and is determined by the clinician

Table 20.6. Physiologic goals of therapy.

Intravascular volume?
Colloid/crystalloid
Myocardial contractility?
Inotropic agents
Systemic vascular resistance?
Vasopressor agents

during assessment of hemodynamic instability. Once specific physiologic goal(s) of therapy are determined, choice of specific therapy may then be contemplated.

20.3.3. Choice of Specific Therapy

Optimization of intravascular volume (preload) requires administration of intravenous crystalloid and/or colloid, enhancing myocardial contractility involves administration of intravenous inotropic agents, and increasing systemic vascular resistance (afterload) requires use of intravenous vasopressor agents. The most commonly utilized inotropic agents and vasopressor agents are listed in Table 20.7.

Dopamine is an endogenous catecholamine and is an immediate precursor of norepinephrine and epinephrine. Its actions are mediated via stimulation of alpha-, beta-, and dopaminergic receptors. In low doses (1–3 mcg/kg/min), dopamine predominantly stimulates dopaminergic receptors. Increasing the dose to 6–14 mcg/kg/min predominantly stimulates beta-receptors and further increases in dosing (>14 mcg/kg/min) leads to exclusive stimulation of alpha-receptors. Such dose-dependent effects of dopamine are not very specific and can be influenced by many factors. Dopamine is unique in comparison with other endogenous catecholomines owing to its effects on the kidneys. It may increase renal artery blood flow by causing direct vasodilation of the afferent arteries and indirect vasoconstriction of the efferent arteries. This results in an increase in glomerular filtration pressure and in glomerular filtration rate.

Dobutamine is a synthetic catecholamine that generally produces dose-dependent increases in cardiac output and reductions in diastolic filling pressures. Its primary physiologic effects are mediated via stimulation of beta-receptors (does possess minimal alpha-receptor activity). Venous return, augmented by adrenergic reduction of venous capacitance, likely contributes to the increase in cardiac output. In addition to increasing contractility, dobutamine may have favorable metabolic effects on ischemic myocardium.

Dopexamine is a relatively newly developed synthetic catecholamine, structurally related to dopamine and dobutamine. The drug stimulates both dopaminergic and beta-receptors. An inhibitory action in the neuronal catecholamine uptake mechanism has also been demonstrated and may account for the positive inotropic action of this drug. Continuous infusion of dopexamine results in systemic and preferential renal vasodilation, causing afterload reduction, increases in cardiac output, and improved renal perfusion. Dopexamine reduces afterload through pronounced systemic arterial vasodilation, increased renal perfusion by selective renal vasodilation, and cardiac stimulation through direct and indirect positive inotropic mechanisms. The increase in cardiac output

Table 20.7. Choice of specific therapy.

Inotropic agents		
Beta-receptor agonists	Phosphodiesterase inhibitors	Miscellaneous
Dopamine	Amrinone	Digitalis preparations
Dobutamine	Milrinone	Thyroid hormone
Dopexamine	Enoximone	Calcium
Epinephrine		
Isoproterenol		
Vasopressor agents		
Alpha-receptor agonists	Arginine vasopressin	Methylene blue
Norepinephrine		
Phenylephrine		

appears to occur predominantly as a result of an increase in heart rate, as stroke volume demonstrates only a minimal change. Dopexamine's physiologic effects are most pronounced when used as a continuous infusion of 1–4 mcg/kg/min.

Epinephrine stimulates both alpha- and beta-receptors in a dose-dependent fashion. The sympathoadrenal (endogenous) secretion of epinephrine is critical to support cardiac contractility, exert tonic control of vascular beds, and modulate the body's "stress response." Epinephrine increases stroke volume and cardiac output in a dose-dependent fashion (10–40 ng/kg/min). However, heart rate may also be increased to unacceptable levels.

Isoproterenol is a potent beta-receptor agonist devoid of alpha-receptor agonist activity. Isoproterenol dilates skeletal, renal, and mesenteric vascular beds and decreases diastolic blood pressure. The drug's potent chronotropic action, combined with the potential to decrease coronary perfusion pressure (via decreased diastolic blood pressure), may limit its usefulness in patients with coronary artery disease. Isoproterenol may be uniquely useful for stimulation of cardiac pacemaker cells in the management of acute bradyarrhythmias or heart block. It reduces refractoriness to conduction and increases automaticity in myocardial tissues. The tachycardia seen with isoproterenol is a result of both direct effects of the drug on the heart and reflex effects caused by peripheral vasodilation. Additional application of isoproterenol has included management of right ventricular dysfunction associated with pulmonary hypertension. However, although isoproterenol is an excellent pulmonary vasodilator, decreases in perfusion pressure (particularly diastolic arterial pressure) may lead to right ventricular ischemia.

Phosphodiesterase inhibitors are noncatecholamine and nonadrenergic agents.[13] Therefore, they do not rely upon beta-receptor stimulation for their positive inotropic activity. As a result, the clinical effectiveness of the phosphodiesterase inhibitors is not altered by previous beta-blockade nor is it reduced in patients who may experience beta-receptor down-regulation. Although the precise mechanism of action of the phosphodiesterase inhibitors has yet to be elucidated, the proposed theory of action involves the inhibition of type III phosphodiesterase found predominantly in cardiac muscle. This inhibition results in a secondary increase in cyclic adenosine monophosphate (cAMP), which leads to an increase in calcium channel entry into the cell, accounting for the positive inotropic action. These agents also produce systemic and pulmonary vasodilation. As a result of this combination of hemodynamic effects (positive inotropic support and vasodilation), the term "inodilator" has been coined to describe this class of drugs. Because these agents exert their hemodynamic effects by a nonadrenergic mechanism of action, when used in combination with traditional beta-receptor agonists, phosphodiesterase inhibitors have been shown to result in an additive effect on myocardial performance. Phosphodiesterase inhibitors decrease pulmonary vascular resistance by both a direct action on the pulmonary vasculature [increasing cyclic guanosine monophosphate (cGMP)] and an indirect effect (increasing cardiac output, decreasing pulmonary artery occlusive pressure).

Digitalis binds to a subunit of sodium potassium ATPase, producing complete inhibition of enzymatic and transport processes. Thus, intracellular sodium and calcium increase and intracellular potassium is lost. The elevated intracellular sodium increases the availability of calcium to the contractile proteins, increasing contractility. Increased intracellular calcium is associated with decreased intracellular pH, which increases inward sodium movement and outward hydrogen ion movement, further increasing intracellular sodium concentration and inotropy. Digitalis exerts its positive inotropic effect independent of catecholamine liberation. Digitalis augments both force and velocity of myocardial contraction without raising cardiac output. Ventricular end-diastolic volume and end-diastolic pressure are decreased. The positive inotropic effects of digitalis, however, are weak. The physiologic onset of action of digitalis occurs within 15–30 min following intravenous administration, with peak effects being obtained in 2–5 h. It must be kept in mind that the therapeutic plasma level "window" of digoxin is relatively narrow and substantial toxicity (heart block, enhanced automaticity) may occur.

Thyroid hormone's effects on the cardiovascular system are well established in clinical states of hyperthyroidism and hypothyroidism. Clinical studies suggest that a reduction in plasma thyroid hormone concentration may be associated with the decreased myocardial performance that occurs in certain clinical scenarios, such as that which occurs following exposure to cardiopulmonary bypass and in the setting of organ transplantation. However, the proper role that thyroid hormone supplementa-

DropBooks

tion plays in clinical treatment of hemodynamic instability remains to be determined.

Calcium may antagonize the action of catecholamine activity, but does not alter the cardiotonic actions of phosphodiesterase inhibitors. Calcium influx during ischemia-reperfusion may increase oxygen consumption and contribute to diastolic dysfunction. However, calcium administration usually increases mean arterial pressure via an increase in systemic vascular resistance and may also improve right ventricular function.

Magnesium has a key role in cellular energy transfer and use (involving adenosine triphosphate) and in cell membrane function. It is widely used as an adjunct for the treatment of arrhythmias following myocardial infarction. Magnesium may influence hemodynamic performance through its modulation of vascular tone, intracellular calcium, catecholamine activity, and adenosine triphosphate metabolism. The potential for magnesium deficiency to affect cardiovascular performance may be particularly relevant in the presence of ischemia, and there are reports of a potential role for magnesium in enhancing hemodynamic performance in ventricular dysfunction following cardiac surgery.

Norepinephrine stimulates both alpha- and beta-receptors in a dose-dependent fashion. Norepinephrine, after a long period of disfavor, is experiencing a renewed popularity for management of hemodynamic instability. When used appropriately, norepinephrine increases blood pressure, increases stroke volume, increases cardiac output, and increases urine output.

Phenylephrine is a potent alpha-receptor agonist devoid of beta-receptor agonist activity. Thus, the physiologic effect of phenylephrine administration is an increase in systemic vascular resistance, with no effects as myocardial contractility.

Arginine vasopressin is an endogenous peptide synthesized exclusively in the hypothalamus and released from the posterior pituitary. Traditionally, arginine vasopressin release is stimulated by changes in vascular volume and vascular tone. Vasopressin is bound by two distinct types of receptors: renal (V2) and vasomotor (V1). Although under normal conditions, arginine vasopressin contributes little, if any, to blood pressure maintenance, investigations have shown the ability of arginine vasopressin to be helpful in the management of certain refractory vasodilatory states.[14,15] In a syndrome known as postconditioning vasodilatory shock (characterized by catecholamine resistance, low systemic vascular resistance despite norepinephrine administration), administration of arginine vasopressin is effective in restoring hemodynamic stability. Numerous investigators have explored the role of arginine vasopressin administration in the management of vasodilatory states in septic shock and following cardiopulmonary bypass. Although the precise mechanisms responsible for this vasodilatory state are unknown, patients experiencing such vasodilatory states are characterized by a significant reduction in circulating vasopressin. In these patients, infusion of arginine vasopressin in the range of 2–8 units/hour results in significant hemodynamic improvements. Increases in the infusion above 8 units/hour provide little added effect.

Recently, several case reports have been described in the literature in which the guanylate cyclase inhibitor methylene blue was successfully administered intravenously to reverse norepinephrine-resistant vasoplegia after cardiopulmonary bypass.[16] The favorable effect of methylene blue in this scenario suggests refractory vasoplegia may reflect a dysregulation of nitric oxide synthesis and vascular smooth muscle cell guanylate cyclase activation. The available data have been obtained from anecdotal case reports only and the effect of methylene blue has not been examined in larger cohorts. Methylene blue has also been used to effectively treat patients with septic shock and low peripheral vascular resistance. A few adverse effects of methylene blue in the treatment of norepinephrine-refractory vasoplegia have been described, such as cardiac arrhythmias, coronary vasoconstriction, decreases in cardiac output, renal blood flow, and mesenteric blood flow, increases in pulmonary vascular pressure and resistance, and deterioration in gas exchange. However, most of these side effects are dose-dependent and do not occur when the dose of methylene blue is not greater than 2 mg/kg.

20.3.4. Assessment of Therapy

Assessment of therapy entails contemplation of the same physiologic parameters (heart rate/rhythm, preload, myocardial contractility, and systemic vascular resistance) that were assessed during the initial period of hemodynamic instability. This will involve reassessment of blood pressure, heart rate/rhythm, level of mental status (if applicable), urine output, central venous pressure, information from a pulmonary artery catheter, and/or information from some form of echocardiography.

20.4. Conclusions

The successful perioperative anesthetic management of patients with heart failure is complex and challenging. In order to ensure acceptable postoperative outcome, a true team approach is required by the surgeon, anesthesiologist, perfusionist, and nursing staff. Anesthesiologists managing these patients need to have extensive knowledge regarding cardiovascular physiology and pharmacology, physiologic effects of anesthetic drugs and techniques on the cardiovascular system, and rational assessment/pharmacologic treatment of hemodynamic instability. Most times, no specific drug or technique is truly indicated. Identified goals (analgesia, amnesia, muscle relaxation) can be safely attained in many ways. In the current era, anesthesiologists managing these extremely sick individuals should possess appropriate skills regarding the use of transesophageal echocardiography, which simplifies hemodynamic instability assessment and may influence surgical management. Once again, identified goals (optimize preload, optimize myocardial contractility, optimize afterload) can be safely attained in many ways. Thus, there is much "art" (which requires extensive clinical experience) to the successful perioperative anesthetic management of patients with heart failure.

DropBooks

Key Points to Remember

- Success in surgery for heart failure owes a lot to the team approach. The cardiac anesthesiologist is a very key part of the team.
- Good communication between the surgeon, anesthesiologist, perfusionist, nurse, etc. is critical to successful operative outcomes.
- Extensive hemodynamic monitoring which includes arterial lines, pulmonary artery catheters, trans-esophageal echocardiography have dramatically improved the methods by which cardiac function is evaluated during surgery.
- Anesthetic techniques utilize drugs that minimize cardiac and circulatory dysfunction.
- The choice, titration and use of inotropes or drugs to support the heart are also made with careful ongoing monitoring of cardiac function.

References

1. Chaney MA. Intrathecal and epidural anesthesia and analgesia for cardiac surgery. *Anesth Analg*. 2006;102:45-64.
2. Chaney MA. Cardiac surgery and intrathecal/epidural techniques: At the crossroads? [editorial]. *Can J Anesth*. 2005;52:783-788.
3. Chaney MA. How important is postoperative pain after cardiac surgery? [editorial]. *J Cardiothorac Vasc Anesth*. 2005;19:705-707.
4. Schwann NM, Chaney MA. No pain, much gain? [editorial]. *J Thorac Cardiovasc Surg*. 2003;126: 1261-1264.
5. Mora Mangano C. Risky business [editorial]). *J Thorac Cardiovasc Surg*. 2003;125:1204-1207.
6. McMurray J, Pfeffer MA. New therapeutic options in congestive heart failure: Part I. *Circulation*. 2002;105:2099-2106.
7. McMurray J, Pfeffer MA. New therapeutic options in congestive heart failure: Part II. *Circulation*. 2002;105:2223-2228.
8. Stevenson LW. Clinical use of inotropic therapy for heart failure: Looking backward or forward? Part I: Inotropic infusions during hospitalization. *Circulation*. 2003;108:367-372.
9. Stevenson LW. Clinical use of inotropic therapy for heart failure: Looking backward or forward? Part II: Chronic inotropic therapy. *Circulation*. 2003;108:492-497.
10. Dalen JE. The pulmonary artery catheter—Friend, foe, or accomplice? *JAMA*. 2001;286:348–350.
11. Hall JB. Use of the pulmonary artery catheter in critically ill patients: Was invention the mother of necessity? *JAMA*. 2000;283:2577-2578.
12. American Society of Anesthesiologists and the Society of Cardiovascular Anesthesiologists Task Force on Transesophageal Echocardiography. Practice guidelines for perioperative transesophageal echocardiography. *Anesthesiology*. 1996;84: 986-1006.
13. Levy JH, Bailey JM, Deeb GM. Intravenous milrinone in cardiac surgery. *Ann Thorac Surg*. 2002;73: 325-330.
14. Dünser MW, Mayr AJ, Ulmer H, et al. Arginine vasopressin in advanced vasodilatory shock: A prospective, randomized, controlled study. *Circulation*. 2003;107:2313-2319.
15. Patel BM, Chittock DR, Russell JA, Walley KR. Beneficial effects of short-term vasopressin infusion during severe septic shock. *Anesthesiology*. 2002;96;576-582.
16. Leyh RG, Kofidis T, Strüber M, et al. Methylene blue: The drug of choice for catecholamine-refractory vasoplegia after cardiopulmonary bypass? *J Thorac Cardiovasc Surg*. 2003;125:1426-1431.

21
Perioperative and ICU Care, Fluid Management, and Renal Support

Rinaldo Bellomo and Patrick Murray

21.1. Introduction

The nonsurgical component of the care of adult patients with cardiac failure undergoing cardiac surgery is probably at least as important to their outcome as the surgery itself.

This component of patient care includes four major aspects:

1. The medical management of their cardiac failure
2. The anesthetic management of the patient during the operation
3. The management of the cardiopulmonary bypass (CPB) aspect of the operation
4. The perioperative management of the patient

The perioperative management of these patients is most complex in the acute phase, either when the patient presents critically ill and requires an urgent operation, or immediately after the operation has been completed and the patient has been admitted to the intensive care unit (ICU). This chapter will focus mostly on the aspects of perioperative care which relate to the acute phase or the subacute phase, while the patient remains critically ill, but will also discuss other general principles of management as they relate to fluid therapy, renal support, and important aspects of the general care of the cardiac surgery patient with heart failure.

21.2. The Preoperative Period

Patients with heart failure (acute or chronic) come to cardiac surgery through several pathways: (1) The outpatient setting; (2) The ward in-patient setting; (3) The coronary care unit (CCU); (4) The ICU; and, uncommonly, (5) the emergency department (ED).

Those patients coming from the outpatient setting (patient source 1) usually have the opportunity to be prepared for surgery in a deliberate and planned fashion. Such planning for surgery should allow the cardiologist, the anesthesiologist, and the cardiac surgeon to consider several aspects of care (Table 21.1). These aspects of care should of course be considered for each patient. However, the time frame available for their assessment or the actual ability to obtain such information or manipulate such aspects of patient care is markedly affected by the presence of an acute situation (patient from source 2–5). In urgent situations, decisions have to be made in a hurry and in the absence of a comprehensive, measured discussion with patient or family that gives them sufficient time to consider further care over weeks or months.

When the patient comes to surgery from the CCU, ICU, or ED, by definition, there must have been a sudden change that requires prompt surgical intervention. Such change may stem from ischemia, ischemia with aggravation of heart failure, worsening of valve function, decompensation of myocardial function, endocarditis, valve rupture, and so on. The treatment must, of course, include (1) Stabilization of the physiological state in order to ensure patient safety, (2) Simultaneous management of the exacerbating condition, and (3) Carefully timed surgical intervention.

No randomized controlled trials exist to specify a particular pathway of management for all conditions. Each must be dealt with using the specific knowledge

TABLE 21.1. Issue to be considered prior to elective surgery for cardiac failure.

1. General issues
Medical history: Previous problems with anesthesia including allergies and current medications; presence of conditions that might affect surgical risk (chronic lung disease, renal disease, liver disease, arrhythmias, hematological disorders, diffuse vascular disease, diabetes, early dementia etc.)
Examination: Stigmata of other important medical conditions (see above)
Biochemistry and general tests: Full blood examination, renal and liver biochemistry, group and cross-match of blood, urinalysis, chest X-ray, electrocardiogram, and, in selected patients, pulmonary function tests and arterial blood gases.
2. Specific issues
Recent use of anticoagulants
Recent use of antiplatelet agents
Current control of heart failure symptoms
Optimization of cardiac failure control with medications
Absence of any currently active infection
3. Cardiological issues
Availability and review of all appropriate imaging modalities
Careful assessment of risk/benefit ratio for the decision to operate
Need to modify medications before surgery (stop clopidogrel or aspirin or warfarin)
4. Surgical issues
Quality of leg veins as conduits
Suitability of radial arteries as conduits
If redo surgery, suitable information of previous operation
Planning of correct approach for a given patient (off-pump vs. on-pump, number of grafts, type of valve surgery, cardioplegic strategy, etc.)

which applies to it. Thus, a given patient may just require antibiotics and optimization of cardiac failure medications, while another will require intubation, mechanical ventilation, inotropic support, intra-aortic baloon counterpulsation, continuous hemofiltration, and even extracorporeal membrane oxygenation (ECMO) or the use of a ventricular assist device.

In fact, the principles which apply to this period are the same that apply to postoperative care and will be described in detail later in this chapter.

21.3. The Immediate Postoperative Period

The most important single predictor of a safe postoperative period is the successful execution of a well-planned and correctly applied operation.

However, even when this is done, patients with heart failure require very careful and skilled medical management. If the operation is ill-conceived or ill-executed, or the patient is extremely ill even before surgery, the patient will experience life-threatening problems that sometimes require extraordinary feats of technology and great teamwork to achieve survival and recovery.

21.3.1. Monitoring and Inotropic Drugs

A patient with heart failure undergoing surgery with CPB will inevitably experience a decrease in myocardial contractility, which, combined with the preoperative state of heart failure, typically mandates the use of inotropic drugs. This decrease in contractility is mediated by complex mechanisms[1,2] and typically results in a progressive decrease in contractility with a nadir in function between 8 and 24 h after cardioplegia, depending on the duration of CPB.

Accordingly, almost all of these patients require inotropic support. Although, no randomized controlled trials exist, in the opinion of the authors it is generally best to monitor cardiac output (CO) in cardiac surgery patients, and it is vital to do so in those who have surgery in the context of impaired preoperative myocardial function (heart failure patients).

Monitoring of CO allows physicians to either prevent or rapidly detect and treat a low cardiac output state (LCOS). Such treatment initially requires a judicious combination of three components: (1) Inotropic drugs; (2) Fluids; (3) Control of heart rhythm and rate (pacing).

There are two major classes of inotropic drugs that can be used in patients with cardiac surgery in the setting of heart failure and/or an LCOS: catecholamines and phosphodiesterase III inhibitors (PDEIs)[3–13] (Table 21.2). More recently, they have been joined by a new class of agents called calcium sensitizers.[14] However, experience with these new inotropic agents in cardiac surgery is limited.[15] These agents have different properties (Table 21.2) and have never been compared in suitably powered randomized controlled trials of heart failure patients to test whether the use of one or the other results in better clinical outcomes. Accordingly, they are typically used according to local (institution) and individual (physician) preferences. In addition, there is no consensus definition of what constitutes the goal of inotropic therapy. In general,

DropBooks

Table 21.2. Inotropic drugs.

Agent	Significant features
Epinephrine	Increases cardiac index (CI) with biphasic effect on SVRI. Produces rise in serum lactate.
Dopamine	Increased SVRI at doses above 5.0 μg/kg/min. Less clinical efficacy than dobutamine, dopexamine, amrinone, or enoximone. Increased incidence of adverse cardiac events than dopexamine.
Dobutamine	Better efficacy than dopamine and epinephrine. Decreases systemic vascular resistance index (SVRI). Tachycardia and tachyarrythmia (especially AF), more common.
Dopexamine	Greater tachycardia than dobutamine. More efficacious and less adverse events than dopamine.
Amrinone	Improved weaning from CPB. Improves CI and decreases SVRI with minimal effects on HR. Reports of thrombocytopenia associated with use.
Enoximone	Significant increase in CI without tachycardia. Decreases SVRI. As effective as dobutamine.
Milrinone	Significant increase in CI without tachycardia. Decreases SVRI. As effective as dobutamine, but less AF. Lusitropic. Improves graft flow. As effective as 20 ppm of inhaled nitric oxide in pulmonary hypertension.

AF atrial fibrillation, *CPB* cardiopulmonary bypass, *HR* heart rate.

however, inotropic agents are administered to deal with an LCOS in order to either prevent it or return cardiac output (CO) to adequate levels to ensure sufficient oxygen delivery to tissues.

No definition of what a LCOS is currently exists. However, it would be reasonable to define it as any LCOS (cardiac index of less than 2.4 L/min/m^2 is used as a criterion in some studies) with evidence of organ dysfunction (e.g., a persistently elevated lactate or a urine output persistently less than 0.5 ml/h for more than 1 h).

Such LCOS can continue for several hours to days, despite optimization of volume status, temporary pacing, exclusion of mechanical factors (e.g., cardiac tamponade), and mechanical assistance with intra-aortic balloon counter pulsation (IABP). Causes for the LCOS are multifactorial, including myocardial ischemia during cross-clamping, reperfusion injury, cardioplegia-induced myocardial dysfunction, activation of inflammatory and coagulation cascades, and unreversed preexisting cardiac disease. LCOS can result in reduced oxygen delivery to vital organs. Such end-organ ischemia will lead to multiorgan failure. Initial organ dysfunction and multiple organ failure are among the main causes of prolonged hospital stay after cardiac surgery and they increase resource use and healthcare costs as well as morbidity and mortality. Optimization of cardiac output and oxygen delivery may, therefore, decrease morbidity and reduce length of stay and remains the cornerstone of hemodynamic management.

It must be emphasized here that a particular value for the cardiac index must always be interpreted within the clinical context. A cardiac index of 1.8 L/min/m^2 may be perfectly adequate in a patient with a normal lactate, a urine output of 1 ml/kg/h and a core temperature of 35.5 °C immediately after transfer to the ICU. In such a patient, hypothermia is likely mostly responsible for decreased metabolic demand and the low value of the cardiac index. Nonetheless, in all patients the cause for the low cardiac index must be diligently sought and dealt with. In particular, one must always be vigilant about the possibility of tamponade, pneumothorax, or other mechanical factors that impede cardiac output. Their diagnosis may require a high index of suspicion, regular patient examination and review, and the prompt use of chest X-rays and echocardiography.

The use of inotropic drugs is often insufficient to restore cardiac output if the patient's heart rate (HR) is not optimized. Patients with cardiac failure who have been on beta-blockers until the time of surgery will often be bradycardic postoperatively and will have a LCOS unless the rate is optimized. This is because CO = stroke volume (SV) × HR.

In these patients, even with inotropic drugs and optimal fluid therapy, SV can only be partially increased; therefore optimal HR is vital. This optimization is best achieved by epicardial pacing of the atria in order to maintain atrial contractility. If the patient has chronic atrial fibrillation (AF), ventricular pacing is necessary to maintain an adequate rate. The importance of pacing in the postoperative period in patients with preoperative heart failure cannot be overemphasized. Pacing not only provides the ability to optimizeHR but also allows the prompt and safe treatment of tachyarrhythmias–like AF, which commonly occurs after cardiac surgery in these patients. In particular, the

availability of pacing makes the use of intravenous amiodarone extremely safe.[16]

Fluid therapy is a source of incessant controversy in the postoperative period because of the lack of randomized controlled trials. Such controversy also arises from the need to individualize care and to change such individualized care dynamically and frequently as the patient's hemodynamic state changes over hours and sometimes days following surgery.[17] However, some comments are in order.

First, there is insufficient evidence that a particular kind of fluid is better than another. A recent large randomized controlled trial in critically ill patients showed no difference in overall outcome between patients treated with saline compared to patients treated with albumin.[18] Accordingly, both colloids and crystalloids are theoretically acceptable choices. However, there is widespread concern about inducing fluid overload states and about the capillary leak state that most cardiac surgery patients experience after CPB. Therefore, most of the fluid literature for cardiac surgery patients appears to preferentially report the use of colloid preparations. These typically include either natural colloids such as albumin or artificial colloid solutions such as starch and gelatin preparations.[19]

Second, there is always controversy about "adequacy of filling" in these patients (i.e., what optimal left or right ventricular end-diastolic volume might be in a given patient at a given time). This is also due to the lack of randomized controlled trials and the dynamic nature of all measurements and physiological states. To this controversy, further uncertainty is added by the fact that myocardial filling cannot be reliably assessed by currently applied forms of hemodynamic monitoring.[20] In particular, standard pulmonary artery technology measures pressures, not volumes. The relationship between pulmonary artery catheter derived pressures and end-diastolic filling volumes is highly unpredictable.[20] New technologies are being applied beyond the traditional pulmonary artery catheter such as pulse contour cardiac output analysis by transpulmonary thermodilution[21] and transesophageal echocardiography.[22] Their usefulness in the ICU and ability to deliver superior outcomes remain unknown. In the opinion of the authors, echocardiography and thermodilution technology are complementary and should be used in unison and together with clinical and laboratory assessment of the patient's condition to help guide hemodynamic management. Importantly, however, and irrespective of echocardiographic findings if a fluid challenge (250 ml of IV colloid bolus over 10–15 min in an adult patient) fails to increase CO by >10% (the general limit of error for CO measurements), then the patient is in the flat portion of the filling volume–cardiac output relationship curve. Further administration of fluid will not benefit such patients and will potentially induce chamber dilatation, decreased endocardial perfusion, pulmonary edema, myocardial edema, and vital organ edema. Thus, it should be avoided. Particularly seductive and misleading is the appearance of an "underfilled" left ventricle on echocardiography in the setting of right ventricular dysfunction with an already enlarged right ventricle and a high right atrial pressure (>15 mmHg). Further filling will predictably result in the following: no change in left ventricular filling, septal movement into the left cavity with decreased left ventricular compliance, further right ventricular dilatation, right ventricular endocardial ischemia, increased back pressure in the liver, liver cell ischemia, and no change or even a decrease in cardiac output. In this setting, the correct treatment is the use of inotropic support, pulmonary vasodilatation with nitric oxide, and, if these measures appear insufficient, institution of mechanical support.

DropBooks

21.3.2. Vasopressor Drugs

Hypotension is relatively common after cardiac surgery. While a degree of hypotension may be clinically unimportant, a low mean arterial blood pressure (MAP < 70 mmHg) may be undesirable in some patients (carotid artery disease, renovascular disease) and, in general, should be prevented or treated. A very low blood pressure (MAP < 60 mmHg or diastolic BP < 40 mmHg) frequently causes renal dysfunction, threatens the adequacy of liver perfusion, and may induce inadequate coronary blood flow with subendocardial ischemia in the setting of high pulmonary artery occlusion pressures (PAOP). In particular, if the diastolic BP is 40 mmHg and the PAOP (a surrogate for left ventricular end diastolic pressure) is 25 mmHg, coronary perfusion pressure for the left ventricle would be 15 mmHg. This value would be <25% of normal and would reduce coronary blood flow

dramatically, especially in a hypertrophic ventricle.[23] The same is true for liver blood flow in the setting of an LCOS, right ventricular dysfunction, and an elevated central venous pressure.[24]

The pathogenesis of hypotension after cardiac surgery in heart failure patients is typically complex and may involve a variety of factors either alone or in combination (Table 21.3). All should be considered and either excluded or identified by means of prompt clinical, radiological, hematological, and hemodynamic assessment.

If the patient has an adequate or even high cardiac output and all other factors have been excluded, then one is dealing with an "inflammatory vasodilatory state" or so-called "post-CPB vasoplegia."[25] In these patients, if the blood pressure is too low, the use of vasopressor drugs becomes necessary. There are several vasopressor agents that can be used for this purpose (norepinephrine, phenylephrine, vasopressin). The agent for which there is greater experience is norepinephrine. Despite concerns over its adverse effects on renal and mesenteric blood flow, most of the available data indicate this agent is efficacious and safe under these circumstances,[26] particularly from the renal functional point of view (Figure 21.1).

In some patients with preoperative sepsis (e.g., endocarditis), the vasodilatory state can be dramatic and may require the addition of vasopressin.[27]

Assuming that external mechanical factors have been corrected, the approach to the hemodynamic management of these patients can be summarized in a flowchart (Table 21.4).

TABLE 21.3. Factors potentially responsible for hypotension after cardiac surgery in heart failure patients.

Low cardiac output syndrome
Relative or absolute hypovolemia
Bleeding
Tamponade
Pneumothorax
Inflammatory response to CPB
Fever
Drugs used for sedation
Use of inodilators (PDEIs)
Residual effect of preoperative ACE inhibitors
Patient-ventilator dyssynchrony

CPB cardiopulmonary bypass, *PDEIs* phosphodiesterase III inhibitors, *ACE* angiotensin-converting enzyme.

21.3.3. Mechanical Support

Some patients with heart failure have severe cardiac functional impairment after surgery. Despite the use of inotropic agents, optimization of fluid therapy, optimization of pacing, and the addition of vasopressor drugs to restore adequate vital organ perfusion pressure and nitric oxide to decrease pulmonary vascular resistance, some of these patients continue to have either an LCOS, hypotension, or both. In these patients, mechanical support should be rapidly considered and implemented.

Broadly speaking, the first line of support is the implementation of IABP. The addition of IABP can sometimes bring about sufficient improvement in hemodynamics and no further mechanical support is needed. However, in general the benefits of IABP in these patients are modest and if there are continuing signs of LCOS,[28] the treating team should rapidly move to more advanced mechanical support, which (depending on the situation, availability, and local expertise) may be in the form of a ventricular assist device, or a total artificial heart device, or the institution of ECMO.[29] Such mechanical devices add another layer of complexity to the management of the patients. The care of such patients requires consideration of a myriad of issues,[29] which cannot be discussed in a general chapter. Nonetheless, it is important to note that almost all of these patients have acute renal failure and requirements for very tight fluid control, especially because the administration of large amounts of blood and blood products is relatively common. As will be discussed in detail later in the chapter, the use of hemofiltration in these patients both during and particularly after surgery offers important physiological advantages (further discussion follows).[30,31]

21.3.4. Nonhemodynamic Issues

Beyond the dominant hemodynamic issues, these patients share several other unique features. One such feature is the risk of postoperative bleeding.[32] Although a variety of steps are typically taken in the OR to prevent this complication, some patients continue to have large mediastinal drainage postoperatively. In these patients, several steps should be promptly considered:

1. Measurement of international normalized ratio (INR), fibrinogen, and activated partial thromboplastin time (APTT)
2. Empiric administration of protamine

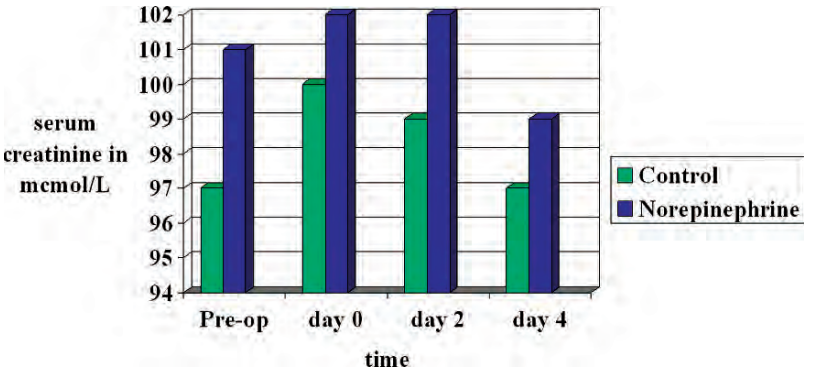


FIGURE 21.1. Comparison of changes in renal function between two groups of patients after cardiac surgery: one treated with norepinephrine, the other without.

TABLE 21.4. Criteria for initiation of CRRT in the cardiothoracic ICU.[80]

Oliguria (urine output < 200 ml/12 h)
Anuria/extreme oliguria (urine output < 50 ml/12 h)
Hyperkalemia (serum K^+ > 6.5 mEq/L)
Severe metabolic acidosis (with pH < 7.1 or base excess < −8 mEq/L)
Azotemia ([urea] > 30 mmol/L)
Major vital organ edema
Suspected uremic encephalopathy
Suspected uremic pericarditis
Suspected uremic neuropathy/myopathy
Severe dysnatremia ([Na^+] >160 or <115 mEq/L)
Hyperthermia (temperature > 40 °C)
Need for massive administration of blood and blood products
Cardiogenic shock requiring mechanical support

CRRT continuous renal replacement therapy, *ICU* intensive care unit.

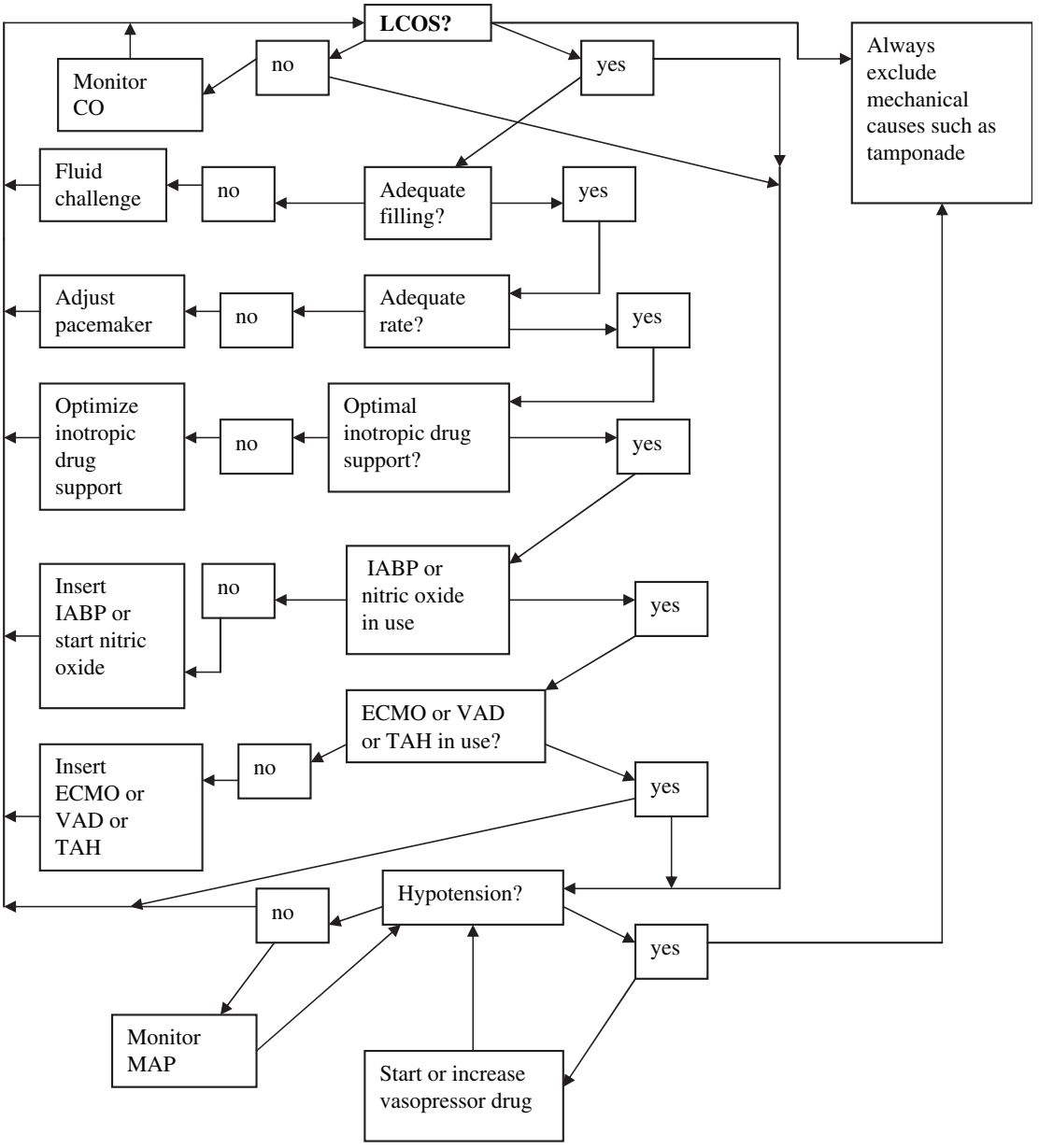
3. Empiric administration of platelets
4. Empiric administration of an antifibrinolytic agent
5. Empiric administration of fresh frozen plasma
6. Empiric administration of cryoprecipitate

The patient should promptly return to the OR for surgical intervention if mediastinal drainage continues at a high rate (e.g., >200 ml/h) despite an aggressive response with platelet administration and near normalization of INR, APTT, and fibrinogen levels, and/or there is suspicion of tamponade or evidence of an accumulating hemothorax.

Another common and unique feature of heart failure patients having cardiac surgery is their high likelihood of developing AF. This is an undesirable complication because it removes the atrial contribution to left ventricular filling in patients who tend to have diastolic dysfunction. Furthermore, if the ventricular response rate is too fast, such ventricular filling will be further impaired by the decreased filling time. Accordingly, it is desirable to prevent AF. Although meta-analysis shows that beta-blockers may reduce the risk of postoperative AF,[33] their use in patients with poor left ventricular function on inotropic agents is fraught with danger. On the other hand, prophylactic magnesium supplementation is exceedingly safe. A meta-analysis of 17 trials using magnesium prophylaxis after cardiac surgery showed a significant 23% reduction in the incidence of supraventricular arrhythmias.[34] Amiodarone is another effective agent which is safer than beta-blockers in these patients. This agent has been repeatedly shown to be effective when given prophylactically, as well as for treatment of new-onset AF.[16] As this agent typically induces a degree of bradycardia, it is at its safest when coupled with the presence of epicardial pacing. Amiodarone also remains an ideal agent for the treatment of essentially all arrhythmias in the postoperative period. Normalization of potassium levels and administration of supplemental magnesium are, in our opinion, vital ancillary measures in these patients. Avoidance of low-dose dopamine use, as discussed below, may also decrease the incidence of perioperative supraventricular arrhythmias.[35,36]

In many other ways, however, cardiac surgery patients with heart failure are similar to critically ill patients with other disorders. First, they require postoperative mechanical ventilation. In most cases such ventilation is straightforward and executed along conventional lines. However, in patients with

DropBooks



LCOS = low cardiac output syndrome; CO = cardiac output; MAP= mean arterial pressure;
IABP = intraaortic balloon counterpulsation; ECMO = extracorporeal membrane oxygenation;
VAD = ventricular assist device; TAH = total artificial heart

FIGURE 21.2. Flow diagram illustrating the principles and steps for a logical approach to hemodynamic management after cardiac surgery.

comorbidities such chronic obstructive pulmonary disease (COPD), suppurative lung disease, or asthma, such ventilation may require specific adjustments. In patients with known right ventricular dysfunction and/or pulmonary hypertension, hypercarbia and acidemia should be prevented or rapidly treated by means of adjusted minute ventilation, because they increase pulmonary vascular resistance and may exacerbate right ventricular failure.

Derangements of acid–base status are frequently observed in patients after cardiac surgery. Their pathogenesis is complex[37]; however, the most common and important disorder is nonanion gap acidosis which is secondary to the effect of the pump prime fluid on the strong ion difference.[38–40] Such acidosis slowly resolves over the first 12–24 h, provided no further chloride-rich fluids are given. It is wise, however, to monitor blood lactate levels on a regular basis, as they are often an early indicator of clinical deterioration.

Many of these patients develop hyperglycemia. A recent single-center randomized controlled trial,[41] which contained close to 500 cardiac surgery patients in each arm, showed that the maintenance of normoglycemia may reduce morbidity and mortality in critically ill patients. Although these findings need to be confirmed in a multicenter setting, it appears desirable to pursue tight glycemic control after cardiac surgery in general and particularly in more complex patients who are likely to have a prolonged ICU and hospital stay.

Infection, especially pulmonary infection, remains an important source of morbidity in these patients and should be considered in the presence of any change in patient status, temperature, or leukocyte count. Although protection from chest infection is typically promoted by the application of breathing exercises and physiotherapy, no evidence of clinical benefit could be demonstrated in a recent randomized controlled trial.[42] Central venous lines or other invasive devices should be removed as soon as possible, to prevent line-related sepsis. Finally, other general measures of patient care should routinely be attended to, including pressure sore prevention, administration of prophylactic gastric acid suppression therapy, the early introduction of deep venous thrombosis prevention, and, in the majority of cases, the administration of aspirin within the first 48 h. Finally, although many patients are able to rapidly resume oral intake after surgery, a significant proportion of patients cannot do so. In such patients, rapid implementation of enteral nutrition is considered important. If gastroparesis is present, the use of nasojejunal feeding may become necessary.[43]

Last, but not the least, pain relief requires careful attention because pain may inhibit coughing and promote chest infection, and because it can trigger patient anxiety, discomfort, and distress and induce significant deleterious hemodynamic changes. Pain control requires the use of judicious combination of approaches from the administration of intravenous narcotics (either under medical direction, or preferably in the form of patient-controlled analgesia), the strict use of acetaminophen, the adjunctive use of nonsteroidal anti-inflammatory drugs in selected patients, the use of low-dose ketamine infusion, and in some cases the use of thoracic epidural analgesia.

As the use of narcotics frequently induces nausea and vomiting, prophylactic or prompt patient-responsive antiemetic treatment is also important.

21.4. Perioperative Renal Dysfunction, Fluid Management, and Renal Support

21.4.1. Impact of Acute Kidney Injury on Outcomes after Cardiac Surgery

Renal dysfunction commonly complicates the perioperative management of cardiac surgery patients, particularly in patients with preexisting congestive heart failure and renal insufficiency. It is increasingly recognized that development of acute kidney injury (AKI) following cardiac surgery portends a poor outcome, so that prevention and aggressive management of this complication are important components of perioperative care in high-risk patients. AKI is common following cardiac surgery, occurring in 7.7%[44]–42%[45] of patients with previously normal renal function, depending on the definition of AKI used. Even small increments in serum creatinine have been shown to be associated with increased mortality after cardiac surgery and other insults.[45–51] There is emerging evidence that any change in serum creatinine may have important prognostic value postcardiac

surgery, including increases barely beyond the limits of assay variability, and even postoperative decrements (perhaps associated with hemodilution in patients with shock).[47] Specifically, postoperative serum creatinine increments of 20–25% are associated with mortality increases from 0–1% to 12–14%,[48,49] and even increments of 0.1–0.3 mg/dL are associated with significant increased mortality.[47] Nonetheless, *severity* of renal dysfunction, and in particular the requirement of dialysis, has major *additional* prognostic significance. Mangano and colleagues found that patients developing severe AKI after cardiac surgery had greatly increased in-hospital mortality (63%) compared to those with nondialyzed AKI (19%) or stable renal function (0.9%).[44] Similarly, in another large study Chertow and colleagues found that the mortality in patients with AKI after cardiac surgery was far higher in those who were dialyzed (63.7%) than in those who were not (4.3%).[46] A study of 2,672 patients who required coronary artery bypass surgery (CABG) showed an incidence of postoperative AKI of 8% with a mortality rate of 14%.[51] There was a 0.7% incidence of postoperative AKI that required dialysis, with a twofold higher mortality rate of 28%. In contrast, the mortality rate of patients without AKI was only 1.8%. Recent data also suggest that postoperative AKI is associated with an increased risk of perioperative infection, further complicating the postoperative course and increasing mortality.[52]

21.4.2. AKI Risk Factors and Risk Stratification

A variety of patient characteristics (chronic kidney disease, CKD; advanced age; diabetes mellitus; congestive heart failure), operative factors (emergent surgery, prolonged CPB time, valvular surgery, repeat CABG), and postoperative events (vasodilatory or cardiogenic shock, bleeding) are known to increase the risk of AKI following cardiac surgery.[44,46,51] The major preoperative/patient risk factors for perioperative AKI include CKD, which is increasingly prevalent among those requiring cardiac surgery. The incidence of severe AKI requiring postoperative renal replacement therapy (RRT) after cardiac surgery is three- to sixfold higher in patients with prior CKD.[46] In a multicenter prospective observational study of 2,222 patients in 24 university hospitals, preoperative factors which predict postoperative renal failure were age older than 70, congestive heart failure, previous myocardial revascularization, type I diabetes mellitus, preoperative serum creatinine between 1.4 and 2 mg/dL, preoperative glucose above 300 mg/dL, and CPB for more than 3 h.[44] In a cohort study of 43,642 patients in 43 Veterans Affairs medical centers who underwent CABG or valvular surgery, the risk factors for perioperative AKI were poor cardiac performance (ejection fraction < 35%, NYHA class IV heart failure, and pulmonary rales), peripheral vascular disease, and reduced renal function.[46] Most recently, Thakar and colleagues at the Cleveland Clinic developed and validated a new score for the prediction of AKI requiring dialysis postcardiac surgery.[53] Among 13 possible AKI score categories, all were assigned 1–2 points from a maximum total of 17, except for preoperative serum creatinine level of ≥ 2.1 mg/dL, which was assigned 5 points. It is clear that preoperative renal insufficiency is the major patient risk factor for severe AKI following cardiac surgery. Among operative risk factors, emergent surgery, prolonged CPB time, and type of surgical procedure (valve + CABG > valve or redo CABG > first-time CABG) have the greatest impact on AKI risk. It remains unclear if avoidance of CPB with off-pump CABG (OPCAB) reduces the risk of AKI, perhaps because perioperative renal hypoperfusion still occurs during this procedure, and may even be more severe without the hemodynamic support of bypass.[54] Finally, patients with postoperative low-cardiac output syndrome, vasodilatory shock,[55] and bleeding are highest risk for postoperative AKI.

21.4.3. AKI Prevention and Pharmacotherapy

Although preoperative identification of patients at high risk of AKI is possible, there are no proven interventions to prevent AKI following cardiac surgery.[56] Efforts to provide effective prophylaxis against AKI in high-risk patients undergoing cardiac surgery (and in other settings) have been hampered by the lack of a standard definition of AKI, by the inadequate sample size in prophylaxis trials that include subjects at low risk of perioperative AKI, and by the lack of early markers of acute renal injury to guide targeting of early interventions.

Careful monitoring of renal function, appropriate use of fluids, vasoactive drugs, and diuretics to optimize renal function, avoidance of nephrotoxins, and appropriate use of RRT are critical approaches to minimize any potential adverse impact of perioperative renal dysfunction on outcomes.

There are some precise experimental data examining the role of perfusion pressure in the pathogenesis of renal dysfunction in CPB patients. Animal studies support the concept that renal blood flow (RBF) during CPB is dependent on renal perfusion pressure,[57] suggesting loss of autoregulation, but pressor-induced increased MAP does not augment renal perfusion if pump flow is low.[58] Similarly, small studies in on-pump CABG patients suggest that increasing MAP by augmenting pump flow or adding a pressor in the presence of normal flow increases renal perfusion, but pressor use is ineffective for this purpose when pump flow is low.[59,60] There has not been a trial of higher versus lower renal perfusion pressure for the prevention of perioperative AKI in CABG patients at risk, and this was not examined as an endpoint in a randomized trial that showed improved cardiovascular and neurologic outcomes with higher perfusion pressures.[61] It is possible that AKI incidence may be reduced by preservation of perfusion pressure during and after CPB, particularly in patients with preexisting hypertension,[62] but this hypothesis has not been tested by prospective, randomized trials.

Studies of pharmacotherapies to prevent or treat AKI after cardiac surgery have generally been negative, or promising pilot study results have not been replicated or followed by subsequent definitive trials of adequate scale. In two randomized, placebo-controlled trials of a total of 204 patients with normal renal function undergoing elective cardiac surgery, the alpha-2 adrenergic agonist clonidine improved perioperative creatinine clearance, along with more hemodynamic stability and reduced surgical stress hormone response.[63,64] There has been no subsequent trial to confirm these promising data. Most perioperative renoprotection trials have focused on renal-specific interventions, including a variety of diuretics and vasodilators. Prophylactic use of loop diuretics in this setting has been found harmful in two clinical studies,[65,66] similar to experimental results in radiocontrast nephropathy prophylaxis. In a double-blind, placebo-controlled trial of 126 patients with normal preoperative renal function randomized to infusions of furosemide infusion, low-dose dopamine or saline (control), 6 of 41 patients who received furosemide developed acute renal injury (defined as an increase of ≥ 0.5 mg/dL in serum creatinine within 48 h postoperatively), versus 1 of 42 in the dopamine group, and none in the saline group ($p < 0.01$).[65] The primary endpoint of maximum increase in serum creatinine within 48 h postoperatively was significantly higher in the furosemide group than in either of the other groups ($p < 0.001$), associated with lower measured creatinine clearances on the 2nd to 4th postoperative days. RRT was required in two patients in the furosemide group, but none in the saline or dopamine groups. Lombardi and colleagues studied 50 adults with baseline serum creatinine values of ≤ 1.5 mg/dL undergoing CPB, all of whom received boluses of furosemide (1 mg/kg) and mannitol (3 mL/kg) at the beginning of bypass, with supplemental furosemide boluses to treat intraoperative oliguria.[66] In multivariate analysis, only baseline serum creatinine and furosemide dose were associated with increased serum creatinine at 24 h postoperatively.

Similarly, there is little evidence of benefit from diuretic therapy in established AKI, following cardiac surgery or in other settings. Loop diuretics are commonly used to "convert" oliguric AKI into nonoliguric AKI, attempting to improve AKI course, and prognosis. In patients with established acute tubular necrosis (ATN), several studies have found no benefit of loop diuretics.[67] Their use did not accelerate renal recovery, decrease the need for dialysis, or reduce mortality, although these trials have been of inadequate size and power. It was shown that the mortality rate of oliguric patients who responded to furosemide with a diuresis was lower than of those who did not. However, the clinical characteristics, severity of renal failure, and mortality rates were similar in patients with either spontaneous nonoliguric AKI or nonoliguric AKI after furosemide. This implies that those patients able to respond to furosemide have less severe renal damage than do nonresponders, rather than deriving any true therapeutic benefit from furosemide administration.

Although administration of furosemide might facilitate improved fluid management if it induces a diuresis, a retrospective review of a recent trial in critically ill patients with ATN raised concerns

DropBooks

of possible harm from loop diuretics in AKI.[68] The authors found that diuretic use was associated with an increased adjusted risk of death and nonrecovery of renal function. Most of the increased risk, however, was seen in those patients unresponsive to high doses of diuretics, implying they had more severe disease. In contrast, in a prospective, 54-center, international study, Bellomo and colleagues found that diuretics were not associated with an increased adjusted mortality risk.[69] In the Beginning and Ending Supportive Therapy for the Kidney (B.E.S.T. Kidney) study, 1,743 consecutive critically ill patients who were treated with RRT or met predefined criteria for severe AKI were prospectively enrolled and followed until hospital discharge or death. Seventy percent of these patients were receiving diuretics at study inclusion, 98.3% receiving furosemide. Unadjusted hospital mortality was significantly higher in diuretic-treated patients (62.4%) than in patients who did not receive diurietics (57.1%; odds ratio, 1.25; $p = 0.03$). However, using two different propensity score-adjusted multivariate models, along with a standard multivariate model with adjustment for collinearity, they found no relationship between diuretic therapy and adjusted hospital mortality (which controlled for other variables). They concluded that there is equipoise, justifying a clinical trial to determine the potential benefit of loop diuretics in AKI.

Finally, a recent randomized controlled trial of loop diuretics in late AKI already starting dialysis showed no survival benefit.[70] Cantarovich and colleagues randomized 388 patients with dialysis-requiring AKI to receive placebo or furosemide (25 mg/kg/day intravenously or 35 mg/kg/day orally, up to maximum doses of 2 or 2.5 g daily, respectively). Furosemide was significantly associated with an increased likelihood of achieving 2 liters of daily urine output (57% vs. 33%), and decreased duration of oliguria with this urine output cutoff (5.7 vs. 7.8 days). The study groups did not differ in time on dialysis, number of dialysis sessions required, renal recovery rates, or survival (the primary endpoint). The only significantly increased side effect was polyuria (7 furosemide subjects, none with placebo, $p = 0.015$), although there was a trend toward more hypokalemia in the furosemide group (11 patients vs. 7 with placebo, $p = 0.07$). Three furosemide patients developed hearing loss, and three developed pancreatitis; one subject had each of these adverse events in the placebo group, which is not significantly different. Based upon these data, there seems little likelihood of benefit from loop diuretic therapy in late AKI requiring RRT.

21.4.3.1. Atrial Natriuretic Peptide

Atrial natriuretic peptide (ANP) has failed to improve outcomes in a radiocontrast nephropathy prophylaxis trial and two trials in patients with ATN. A new, promising, but underpowered study of ANP to treat AKI immediately following cardiac surgery showed a decreased rate of postoperative RRT compared to placebo-treated patients.[71] In this study, Sward and colleagues randomized 61 patients with AKI following cardiac surgery (defined as a serum creatinine increase of ≥50% from a baseline value of <1.8 mg/dL) to receive infusion of ANP or placebo until the serum creatinine decreased below the baseline value at enrollment, the patient died, or one of four prespecified dialysis criteria was reached. Of note, all patients received infusions of furosemide (20–40 mg/h) and oliguria, defined as a urine output of ≤0.5 ml/kg/h for 3 h, was an exclusion criterion and an automatic dialysis indication. The primary endpoint was the rate of dialysis within 21 days of enrollment. Creatinine clearance was significantly higher on the third study day in ANP-treated subjects ($p = 0.04$). Using prespecified dialysis criteria, 21% of patients in the ANP group and 47% in the placebo group were dialyzed within 21 days (hazard ratio 0.28; 95% CI, 0.10–0.73, $p = 0.009$). The combined secondary endpoint of death-or-dialysis was similarly improved in the ANP group (28%) compared to placebo (57%; hazard ratio 0.35; 95% CI 0.14–0.82; $p = 0.017$. The incidence of hypotension during the first 24 h was 59% in the ANP group and 52% in controls (p = NS). It is intriguing to speculate on the potential reasons for the positive outcome of this trial, compared to larger prior studies of ANP for AKI prevention and therapy. Apart from the possibility that this is a false-positive, underpowered study, possible explanations include the use of ANP earlier in the course of AKI (the mean serum creatinine in the prior ANP studies was much higher), and at lower doses (50 ng/kg/min vs. 200 ng/kg/min) that avoided the significant rate of hypotension observed in prior trials. The use of prespecified dialysis criteria was another strength of

this trial. This study suggests that ANP (and perhaps other vasodilators used at low doses) may have a role in the therapy of early AKI following cardiac surgery, but further prospective trials are needed to confirm this potential indication.

21.4.3.2. Dopaminergic Agonists

Dopamine has been studied extensively to prevent and treat AKI after cardiac surgery, in a variety of small, generally negative studies.[72,73] Furthermore, a recent analysis of 1,731 cases over 2 years in a CABG registry found that renal-dose dopamine was associated with a 1.74 odds ratio of developing postoperative AF or flutter post-CABG surgery.[35] This confirms a prior study by Chiolero and colleagues in which dopamine therapy was the most significant predictor of postoperative arrhythmias after cardiac surgery.[36] Thus, the literature continues to argue against the use of low-dose dopamine in this, as in other settings.

Fenoldopam mesylate is a pure dopamine type-1 receptor agonist that has similar hemodynamic effects to dopamine in the kidney without systemic α- or β-adrenergic stimulation.[74] Animal experiments[75] and small human studies in patients undergoing CABG[76] and aortic cross-clamp surgery[77] suggest that fenoldopam may prevent or ameliorate the course of AKI in patients undergoing cardiovascular surgery. In a small prospective study of fenoldopam in 28 patients who underwent elective aortic surgery, creatinine clearance decreased from 83 to 42 ml/min in those who received saline but not in those who received fenoldopam.[77] Similarly, in a 31-patient study, Halpenny and colleagues showed that fenoldopam transiently improved creatinine clearance after cardiac surgery.[76] In a prospective, randomized, double-blind trial, 80 patients undergoing cardiac surgery were randomized to 24 h of perioperative therapy with low doses of fenoldopam or dopamine.[78] There was no difference between the groups in AKI rate, serum creatinine levels, or a variety of clinical endpoints. Larger prospective, controlled trials in aortic occlusive and cardiac surgeries are required to determine potential indications for prevention or therapy of perioperative AKI. It is important to emphasize that because fenoldopam causes dose-dependent systemic vasodilatation (beginning at a dose of ~0.1 μg/kg/min), renal vasodilatation may be accompanied by hypotension, and extreme caution must be exercised in the experimental or therapeutic use of this drug, especially in critically ill patients.

21.4.4. Renal Replacement Therapy

Cardiac surgery patients commonly develop oliguria, acidosis, or azotemia in the perioperative period, and many groups claim superior outcomes with aggressive use of RRT in this setting.[30,31] There are no adequate controlled trials to guide the timing of RRT initiation in patients with AKI following cardiac surgery, which remains a matter of clinical judgment. The indications for initiation of RRT for patients with AKI following cardiac surgery are a source of considerable clinical controversy in many medical centers. The literature informing this debate is limited, generally composed of uncontrolled studies, some supporting aggressive use of RRT in the perioperative period. One recent study found that a period of "prophylactic" dialysis for patients with chronic renal impairment may subsequently improve both renal and overall outcome.[79] In a study of 44 patients with chronic renal failure (mean serum creatinine level of 3.3 mg/dL) undergoing coronary artery bypass grafting with CPB, randomization to prophylactic hemodialysis appeared to decrease mortality, hospital and ICU length of stay, and the incidence of postoperative AKI compared to standard care. Specifically, 1 of 21 patients who received hemodialysis twice within 72 h before surgery developed AKI, compared to 14 of 23 patients who did not.[79] However, the study was small, details of medical therapy in the nondialysis arm were not described, and this approach requires further research. Similarly, although several studies have demonstrated apparent physiologic advantages to the use of intraoperative hemofiltration,[30,80–82] the strategy is unproven to improve morbidity and survival. Suggested advantages include control of fluid balance, less hemodilution and anemia, and perhaps shorter duration of postoperative mechanical ventilation. Potential mechanisms of benefit include ultrafiltration to control fluid balance, clearance of inflammatory cytokines by hemofiltration, and perhaps adsorptive mediator clearance as well.

In the postoperative period, there is a well-recognized lack of consensus on appropriate indications for RRT initiation in AKI, leading to wide variability in prac-

DropBooks

tice patterns. Several nonrandomized, uncontrolled studies have purported to show that early and aggressive use of RRT improved survival in AKI following cardiac surgery,[31,83–85] but this approach has not been tested in a definitive trial. However, it is our belief that aggressive use of continuous renal replacement therapy (CRRT) in the perioperative period is a necessity for management of high-risk cardiac surgery patients. While there is a lack of consensus on definitive, outcome-based indications for acute RRT, numerous clear-cut physiological indications for RRT develop in many high-risk cardiac surgery patients in the perioperative period. For example, take the illustrative case of a 25-year-old Asian female who undergoes cardiac surgery for congenital heart disease with pulmonary hypertension and severe right heart failure, which is associated with chronic renal insufficiency (baseline serum creatinine 2.5 mg/dL). After 4 h of CPB, it is difficult to wean her from the pump. She returns to the ICU intubated, anuric on furosemide 20 mg/h. Her blood pressure is 80/50 mmHg on vasopressin, dopamine, and norepinephrine infusions. She is mechanically ventilated and has an oxygen saturation 90% on a fractional inspired oxygen of 0.6 with 15 cm H_2O positive end expiratory pressure (PEEP) and inhaled nitric oxide therapy. Central venous pressure is 35 mmHg and venous oxygen saturation is 50%. Her weight is increased 15 kg from preoperatively, and the sternal wound has not been closed because of massive edema. Her chest X-ray demonstrates bilateral pulmonary edema. Her serum creatinine is 2.8 mg/dL. Other laboratory tests disclosed the following values: sodium 135 mEq/L, potassium 4.5 mEq/L, chloride 100 mEq/L, total CO_2 12 mEq/L, blood urea nitrogen (BUN) 70 mg/dL, and glucose 80 mg/dL. Urinalysis is not available. The surgical team plans to transfuse six units of fresh frozen plasma in preparation for return to the operating room for placement of a right ventricular assist device and sternal closure. The nephrology consultant is asked to initiate emergent RRT.

In our opinion, iniation of RRT with CRRT (CVVHD), continuous veno-venous hemofiltration (CVVH), or continuous veno-venous hemodiafiltration (CVVHDF) is the most appropriate choice of intervention for this hemodynamically unstable patient with renal insufficiency, diuretic-refractory oliguria, and severe volume overload. Volume overload is contributing to pulmonary dysfunction, inability to achieve sternal wound closure (with increased risk of mediastinitis), and possibly even to right-sided cardiac dysfunction and shock. Even with maximal response, it is highly unlikely that diuresis can correct volume overload in a timely fashion, particularly in someone refractory to furosemide infusion of 20 mg/h. Slow continuous ultrafiltration (SCUF) will not correct metabolic acidosis, or provide therapy for evolving azotemia glomerular filtration rate (GFR) in this anuric patient is zero). Although serum creatinine has not yet increased significantly to reflect evolving acute-on-chronic renal failure in this patient, there is a strong multipurpose rationale to initiate RRT at this time. Pending validation by adequate prospective trials, we propose the use of liberal criteria for CRRT initiation is cardiac surgery patients with renal dysfunction in the perioperative period, guided by physiological principles and clinical judgment.

21.5. The Prolonged ICU Stay of the Complicated Patient

If the critically ill cardiac failure patient survives the initial hemodynamic instability of the first 48 h after surgery and begins to improve, such improvement may be rapid and lead to ICU discharge over the ensuing day or two. However, some patients remain critically ill, dependent on either inotropic support or mechanical support. They progress only slowly to be weaned serially off mechanical support, then inotropes and vasopressor support. Such patients are exposed to complications similar to those seen in other acutely ill patients who require prolonged intensive care support. Although there are many issues that require discussion, in this chapter, we will focus on some particularly important ones.

First, these patients are at incredibly high risk of infection, particularly if they develop acute renal failure.[52] This is in part because of the highly invasive nature of both monitoring and mechanical support. These critically ill patients will often have several intravenous catheters, an arterial catheter to monitor blood pressure, an IABP device, and, in some cases, large cannulae for mechanical support of cardiac output. They will also have hematomas or some residual clot in the mediastinum and, sometimes, chest drains. All such breaches of skin integrity occur in patients whose immune system is highly dysfunctional

as a consequence of the insults associated with repeated major surgery and an LCOS, as well as renal failure in many cases. In these patients, the onset of sepsis can be lethal. Accordingly, vigilance for possible infection must be extreme. Regular monitoring of sputum for organisms, rapid line change at even minute indications of possible infection (increase in white cell count, change in C-reactive protein, increased body temperature), or even broad-spectrum prophylactic antibiotic cover should all be considered.

As discussed above, careful fluid management is paramount as these patients are at high risk of the acute respiratory distress syndrome. Accordingly, detailed monitoring of fluid balance and use of diuretics and/or hemofiltration are essential tools to avoid unnecessary fluid overload. Mechanical ventilation should be with low tidal volumes.[86]

Almost all of these patients develop anemia. While it is obvously vital that red cell transfusion should take place in the context of continued documented blood loss during various operations, the treatment of anemia of critical illness should preferably be conservative as shown by a recent randomized controlled trial.[87]

In addition to their other problems, these very ill patients are likely to develop a polyneuropathy of critical illness, especially if neuromuscular blocking agents are used.[88] Accordingly, such agents should be used very sparingly.

Last but not the least, there remains the issue of sedation during mechanical ventilation. Once again, such sedation is necessary for patient safety and comfort, as is occasionally true of neuromuscular blockade. However, like neuromuscular blockade, it can be a double-edged sword and lead to the unnecessary prolongation of mechanical ventilation with its attendant problems.[89] Therefore, it should be used judiciously and with the understanding that in the presence of renal failure or hepatic dysfunction, there is significant accumulation of metabolites of sedating agents such as midazolam, which would further prolong the duration of sedation even after cessation of drug infusion. Accordingly, it appears desirable to reassess the patient's needs for sedation daily and to titrate such sedation according to validated sedation scales in order to avoid both under- and overdosage.

Key Points to Remember

- Components of patient care that aid in perioperative care include management of heart failure, anesthetic management during the operation, management of cardiopulmonary bypass and post-operative care.
- The pre-operative period can be frequently used to optimize the patient's condition and improve management of heart failure.
- The immediate post-operative period is a time when there can be great fluctuations, requiring intensive monitoring and frequent interventions.
- Careful attention to cardiac function and the circulatory state is very important.
- Pro-active management of fluids and renal function is a major factor that influences survival in these sick patients.
- End-organ dysfunction such as renal failure carry a high morbidity and mortality in patients with heart failure that undergo cardiac surgery.

DropBooks

References

1. Lalu MM, Pasini E, Schulze CJ, et al. Ischemia-reperfusion injury activates matrix metalloproteinases in the human heart. *Eur Heart J*. 2005;26:27-35.
2. Scarabelli TM, Pasini E, Ferrari G, et al. Warm blood cardioplegic arrest induces mitochondrial-mediated cardiomyocyte apoptosis associated with increased urocortin expression in viable cells. *J Thorac Cardiovasc Surg*. 2004;128:364-371.
3. Boldt J, Hammermann H, Hempelmann G. What is the place of the phosphodiesterase inhibitors? *Eur J Anaesthesiol*. 1993;8:33-37.
4. Feneck RO, Sherry KM, Withington PS, Oduro-Dominah A, European Milrinone Multicenter Trial Group. Comparison of the haemodynamic effects of milrinone with dobutamine in patients after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2001;15:306-315.
5. Polonen P, Ruokonen E, Hippelainen M, Poyhonen M, Takala J. A prospective, randomised study of goal-oriented haemodynamic therapy in cardiac surgical patients. *Anesth Analg*. 2000;90:1052-1059.
6. Lobato EB, Gravenstein N, Martin TD. Milrinone, not epinephrine, improves left ventricular compliance

after cardiopulmonary bypass. *J Cardiothorac Vasc Anesth*. 2000;14:374-377.
7. Butterworth JF 4th, Prielipp RC, Royster RL, et al. Dobutamine increases heart rate more than epinephrine in patients recovering from aortocoronary bypass surgery. *J Cardiothorac Vasc Anesth*. 1992;6:535-541.
8. Myles PS, Buckland MR, Schenk NJ, et al. Effect of "renal-dose" dopamine on renal function following cardiac surgery. *Anaesth Intensive Care*. 1993;21: 56-61.
9. Romson JL, Leung JM, Bellows WH, et al. Effects of dobutamine on hemodynamics and left ventricular performance after cardiopulmonary bypass in cardiac surgical patients. *Anesthesiology*. 1999;91:1318-1328.
10. Dupuis JY, Bondy R, Cattran C, Nathan HJ, Wynands JE. Amrinone and dobutamine as primary treatment of low cardiac output syndrome following coronary artery surgery: A comparison of their effects on hemodynamics and outcome. *J Cardiothorac Vasc Anesth*. 1992;6:542-553.
11. Hurley J, McDonagh P, Cahill M, et al. The haemodynamic effect of prophylactic peri-operative dopexamine in coronary artery bypass patients. *Eur Heart J*. 1995;16:1705-1709.
12. Doolan LA, Jones EF, Kalman J, Buxton BF, Tonkin AM. A placebo-controlled trial verifying the efficacy of milrinone in weaning high-risk patients from cardiopulmonary bypass. *J Cardiothorac Vasc Anesth*. 1997;11:37-41.
13. George M, Lehot JJ, Estanove S. Haemodynamic and biological effects of intravenous milrinone in patients with a low cardiac output syndrome following cardiac surgery: Multicentre study. *Eur J Anaesthesiol*. 1992;5:31-34.
14. Follath F, Cleland JG, Just H, et al. Efficacy and safety of intravenous levosimendan compared with dobutamine in severe low-output heart failure (the LIDO study): A randomized double-blind trial. *Lancet*. 2002;360(9328):196-202.
15. Labriola C, Siro-Brigiani M, Carrata F, Santangelo E, Amantea B. Hemodynamic effects of levosimendan in patients with low-output heart failure after cardiac surgery. *Int J Clin Pharmacol Ther*. 2004;42:204-211.
16. Kerstein J, Soodan A, Qamar M, et al. Giving IV and oral amiodarone perioperatively for the prevention of post-operative atrial fibrillation in patients undergoing coronary artery bypass surgery. *Chest*. 2004;126:716-724.
17. Bellomo R. Fluid resuscitation: Colloids vs. crystalloids. *Blood Purif*. 2002;20:239-242.
18. Finfer S, Bellomo R, Boyce N, French J, Myburgh J, Norton R. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med*. 2004;350:2247-2256.
19. Van der Linden PJ, De Hert SG, Daper A, et al. 2.5% urea-linked gelatin is as effective as 6% HES 200/0.5 for volume management in cardiac surgery patients. *Can J Anaesth*. 2004;51:236-241.
20. Bellomo R, Uchino S. Cardiovascular monitoring tools: Use and misuse. *Curr Opin Crit Care*. 2003;9:225-229.
21. Reuter DA, Felbinger TW, Schmidt C, et al. Stroke volume variations for assessment of cardiac responsiveness to volume loading in mechanically ventilated patients after cardiac surgery. *Intensive Care Med*. 2002;28:392-398.
22. Bettex DA, Hinselmann V, Hellerman JP, et al. Transesophageal echocardiography is unreliable for cardiac output assessment after cardiac surgery compared with thermodilution. *Anaesthesia*. 2004;59:1184-1192.
23. Duncker DJ, Zhang J, Pavek TJ, et al. Effect of exercise on coronary pressure-flow relationship in hypertrophied left ventricle. *Am J Physiol*. 1995;269:H271-H281.
24. Raman J, Kochi K, Morimatsu H, Buxton B, Bellomo R. Severe ischemic early liver injury after cardiac surgery. *Ann Thor Surg*. 2002;74:1601-1606.
25. Mekontso-Dessap A, Houel R, Soustelle C, et al. Risk factors for post-cardiopulmonary bypass vasoplegia in patients with preserved left ventricular function. *Ann Thorac Surg*. 2001;71:1428-1432.
26. Morimatsu M, Uchino S, Chung J, Bellomo R, Raman J, Buxton B. Norepinephrine for severe vasodilatation after cardiac surgery: Impact on renal function. *Intensive Care Med*. 2003;29:1106-1112.
27. Lechner E, Dickerson HA, Fraser CD Jr, Chang AC. Vasodilatory shock after surgery for aortic valve endocarditis: Use of low-dose vasopressin. *Pediatr Cardiol*. 2004;25:558-561.
28. Davies A, Bellomo R, Raman JS, Gutteridge G, Buxton B. An elevated lactate is a useful predictor of mortality during intra-aortic balloon pumping in cardiac surgical patients. *Ann Thorac Surg*. 2000;71:1415-1420.
29. Smith C, Bellomo R, Raman J, et al. The outcome of an integrated ECMO-based approach to post-cardiotomy cardiogenic shock in an older population. *Ann Thorac Surg*. 2000;71:1421-1427.
30. Raman J, Hata M, Bellomo R, Kochi K, Cheung H, Buxton B. Hemofiltration during prolonged cardiopulmonary bypass. *Int J Artif Organs*. 2003;26:753-757.

31. Bent P, Tan HK, Bellomo R, et al. Early and intensive continuous veno-venous hemofiltration for severe acute renal failure after cardiac surgery. *Ann Thorac Surg*. 2001;71:832-837.
32. Liu G, McNicol L, McCall P, et al. Prediction of the mediastinal drainage after coronary artery bypass surgery. *Anaesth Intensive Care*. 2000;28: 420-426.
33. Kowey PR, Taylor JE, Rials SJ, et al. Meta-analysis of the effectiveness of prophylactic drug therapy in preventing supraventricular arrhthmia early after coronary bypass surgery. *Am J Cardiol*. 1992;69:963-965.
34. Shiga T, Wajima Z, Inoue T, Oagawa R. Magnesium prophylaxis for arrhythmias after cardiac surgery: A meta-analysis of randomized controlled trials. *Am J Med*. 2004;117:325-333.
35. Argalious M, Motta P, Khandwala F, et al. "Renal dose" dopamine is associated with the risk of new-onset atrial fibrillation after cardiac surgery. *Crit Care Med*. 2005;33:1327-1332.
36. Chiolero R, Borgeat A, Fisher A. Postoperative arrhythmias and risk factors after open heart surgery. *Thorac Cardiovasc Surg*. 1991;39:81-81.
37. Opdam H, Bellomo R. Oxygen consumption and lactate release by the lung after cardiopulmonary bypass and during septic shock. *Crit Care Resusc*. 2000;2:181-187.
38. Hayhoe M, Bellomo R. The pathogenesis of acid-base changes during cardiopulmonary bypass. *Curr Opin Crit Care*. 1999;5:464-467.
39. Hayhoe M, Bellomo R, Liu G, Kellum JA, McNicol L, Buxton B. The role of the splanchnic circulation in acid-base balance during cardiopulmonary bypass. *Crit Care Med*. 1999;27:2671-2677.
40. Liskaser F, Bellomo R, Hayhoe M, et al. Role of pump prime in the etiology and pathogenesis of cardiopulmonary bypass-associated acidosis. *Anesthesiology*. 2000;93:1170-1173.
41. Van den Berghe G, Wouters P, Weekers F, et al. Intensive insulin therapy in critically ill patients. *N Engl J Med*. 2001;345:1359-1367.
42. Brasher PA, McClelland KH, Denehy L, Story I. Does removal of deep breathing exercises from a physiotherapy program including pre-operative education and early mobilization after cardiac surgery alter patient outcomes? *Aust J Physiother*. 2003;49:165-173.
43. Davies A, Froomes P, French C, *Bellomo R*, et al. Randomized comparison of nasojejunal and nasogastric feeding in critically ill patient. *Crit Care Med*. 2002;30:586-590.
44. Mora Mangano C, Diamondstone LS, Ramsey JG, et al. Renal dysfunction after myocardial revascularization: Risk factors, adverse outcomes, and hospital resource utilization. *Ann Intern Med*. 1998;128:194-203.
45. Tuttle KR, Worrall NK, Dahlstrom LR, et al. Predictors of ARF after cardiac surgical procedures. *Am J Kidney Dis*. 2003;41:76-83.
46. Chertow GM, Lazarus JM, Christiansen CL, et al. Preoperative renal risk stratification. *Circulation*. 1997;95:878-884.
47. Lassnigg AL, Schmidlin D, Mouhieddine M, et al. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: A prospective cohort study. *J Am Soc Nephrol*. 2004;15:1597-1605.
48. Ryckwaert F, Boccara G, Frappier J-M, et al. Incidence, risk factors, and prognosis of a moderate increase in plasma creatinine after cardiac surgery. *Crit Care Med*. 2002;30:1495-1498.
49. Loef BG, Epema AH, Smilde TD, et al. Immediate postoperative renal function deterioration in cardiac surgical patients predicts in-hospital mortality and survival. *J Am Soc Nephrol*. 2005;16:195-200.
50. Leacche M, Rawn JD, Mihalijevic T, et al. Outcomes in patients with normal serum creatinine and with artificial renal support for acute renal failure developing after coronary artery bypass grafting. *Am J Cardiol*. 2004;93:353-356.
51. Conlon P, Stafford-Smith M, White W, et al. Acute renal failure following cardiac surgery. *Nephrol Dial Transplant*. 1999;14:1158-1162.
52. Thakar CV, Yared JP, Worley S, et al. Renal dysfunction and serious infections after open heart surgery. *Kidney Int*. 2003;64:239-246.
53. Thakar CV, Arrigain S, Worley S, et al. A clinical score to predict acute renal failure after cardiac surgery. *J Am Soc Nephrol*. 2005;16:163-169.
54. Schwann NM, Horrow JC, Strong MD, et al. Does off-pump coronary artery bypass reduce the incidence of clinically evident renal dysfunction after multivessel myocardial revascularization? *Anesth Analg*. 2004;99:959-964.
55. Ruel M, Khan TA, Voisine P, et al. Vasomotor dysfunction after cardiac surgery. *Eur J Cardiothorac Surg*. 2004;26:1002-1014.
56. Tang I, Murray PT. Prevention of perioperative ARF: What Works? *Best Pract Res Clin Anaesthesiol*. 2004;18:91-111.
57. Mackay JH, Feerick AE, Woodson LC, et al. Increasing organ blood flow during cardiopulmonary bypass in pigs: Comparison of dopamine and perfusion pressure. *Crit Care Med*. 1995;23: 1090-1098.
58. O'Dwyer C, Woodson LC, Conroy BP, et al. Regional perfusion abnormalities with phenylephrine during normothermic bypass. *Ann Thorac Surg*. 1997;63:728-735.
59. Urzua J, Tronscoso S, Bugedo G, et al. Renal function and cardiopulmonary bypass: Effect of

perfusion pressure. *J Cardiothorac Vasc Anesth*. 1992;6:299-303.
60. Andersson LG, Bratteby LE, Ekroth R, et al. Renal function during cardiopulmonary bypass: Influence of pump flow and systemic blood pressure. *Eur J Cardiothorac Surg*. 1994;8:597-602.
61. Gold JP, Charlson ME, Williams-Russo P, et al. Improvement of outcomes after coronary artery bypass: A randomized trial comparing intraoperative high versus low mean arterial pressure. *J Thorac Cardiovasc Surg*. 1995;110:1302-1314.
62. Aronson S, Boisvert D, Lapp W. Isolated systolic hypertension is associated with adverse outcomes from coronary artery bypass surgery. *Anesth Analg*. 2002;94:1079-1084.
63. Kulka PJ, Tryba M, Zenz M. Preoperative alpha-2 adrenergic receptor agonists prevent the deterioration of renal function after cardiac surgery: Results of a randomized, controlled trial. *Crit Care Med*. 1996;24:947-952.
64. Myles PS, Hunt JO, Holdgaard HO, et al. Clonidine and cardiac surgery: Haemodynamic and metabolic effects, myocardial ischaemia and recovery. *Anaesth Intensive Care*. 1999;27:137-147.
65. Lassnigg A, Donner E, Grubhofer G, et al. Lack of renoprotective effects of dopamine and furosemide during cardiac surgery. *J Am Soc Nephrol*. 2000;11:97-104.
66. Lombardi R, Ferreiro A, Servetto C. Renal function after cardiac surgery: Adverse effect of furosemide. *Ren. Fail*. 2003;25:775-786.
67. Schetz M. Should we use diuretics in acute renal failure? *Best Pract Res Clin Anaesthesiol*. 2004;18:75-89.
68. Mehta RL, Pascual MT, Soroko S, Chertow GM, and the PICARD Study Group. Diuretics, mortality, and nonrecovery of renal function in acute renal failure. *JAMA*. 2002;288:2547-2553.
69. Uchino S, Doig GS, Bellomo R, et al. Diuretics and mortality in acute renal failure. *Crit Care Med*. 2004;32:1669-1677.
70. Cantarovich N, Rangoonwala B, Lorenz H, et al. High-dose furosemide for established ARF: A prospective, randomized, double-blind, placebo-controlled, multicenter trial. *Am J Kidney Dis*. 2004;44:402-409.
71. Sward K, Valsson F, Odencrants P, et al. Recombinant human atrial natriuretic peptide in ischemic acute renal failure. A randomized placebo controlled trial. *Crit Care Med*. 2004 32:1310-1315.
72. Woo EBC, Tang ATM, El Gamel A, et al. Dopamine therapy for patients at risk of renal dysfunction following cardiac surgery: Science or fiction? *Eur J Cardiothorac Surg*. 2002;22:106-111.
73. Tang ATM, El-Gamel A, Keevil B, et al. The effect of "renal-dose" dopamine on renal tubular function following cardiac surgery: Assessed by measuring retinol binding protein (RBP). *Eur J Cardiothorac Surg*. 1999;15:717-722.
74. Murray PT. *Use of Dopaminergic Agents for Renoprotection in the ICU. Yearbook of Intensive Care and Emergency Medicine*. Springer-Verlag; 2003:637-648.
75. Halpenny M, Markos F, Snow HM, et al. The effects of fenoldopam on renal blood flow and tubular function during aortic cross-clamping in anaesthetized dogs. *Eur J Anaesth*. 2000;17:491-498.
76. Halpenny M, Lakshmi S, O' Donnell A, et al. Fenoldopam: Renal and splanchnic effects in patients undergoing coronary artery bypass grafting. *Anaesthesia*. 2001;56:953-960.
77. Halpenny M, Rushe C, Breen P, et al. The effects of fenoldopam on renal function in patients undergoing elective aortic surgery. *Eur J Anesth*. 2002;19:32-39.
78. Bove T, Landoni G, Calabro MG, et al. Renoprotective action of fenoldopam in high-risk patients undergoing cardiac surgery. A prospective, double-blind, randomized clinical trial. *Circulation*. 2005;111:3230-3235.
79. Durmcaz I, Yagdi T, Calkaur T, et al. Prophylactic dialysis in patients with renal dysfunction undergoing on-pump coronary artery bypass surgery. *Ann Thorac Surg*. 2003;75:859-864.
80. Bellomo R, Raman J, Ronco C. Intensive care unit management of the critically ill patient with fluid overload after open heart surgery. *Cardiology*. 2001;96:169-176.
81. Oliver WC, Nuttall GA, Orszulak TA, et al. Hemofiltration but not steroids results in earlier tracheal extubation following cardiopulmonary bypass: A prospective, randomized double-blind trial. *Anesthesiology*. 2004;101:327-339.
82. Chew MS. Does modified ultrafiltration reduce the systemic inflammatory response to cardiac surgery with cardiopulmonary bypass? *Perfusion*. 2004;19: S57-S60.
83. Demirkilic U, Kuralay E, Yenicesu M, et al. Timing of replacement therapy for acute renal failure after cardiac surgery. *J Card Surg*. 2004;19:17-20.
84. Elahi MM, Lim MY, Joseph RN, et al. Early hemofiltration improves survival in post-cardiotomy patients with acute renal failure. *Eur J Cardiothorac Surg*. 2004;26:1027-1031.
85. Sugahara S, Suzuki H. Early start on continuous hemodialysis therapy improves survival rate in patients with acute renal failure following coronary bypass surgery. *Hemodial Int*. 2004;8:320-325.
86. Bersten AD, Edibam C, Hunt T, et al. Incidence and mortality of acute lung injury and the acute respiratory distress syndrome in three Australian states. *Am J Respir Crit Care Med*. 2002;165:443-448.

87. Hebert PC, Wells G, Blajchman MA, et al. A multicentre, randomized controlled clinical trial of transfusion requirements in critical care. *N Engl J Med*. 1999;340:409-417.
88. Vanderheyden BA, Reynolds HN, Gerold KB, et al. Prolonged paralysis after long-term vecuronium infusion. *Crit Care Med*. 1992;20: 304-307.
89. Koleff MH, Levy NT, Ahrens TS, et al. The use of continuous IV sedation is associated with prolonged mechanical ventilation. *Chest*. 1998;114: 541-548.

DropBooks

22
New Therapies and What Is on the Horizon

Keiichi Tambara and Masashi Komeda

22.1. Range of New Therapies

In the last decade, several new treatment strategies have emerged in the surgical management of heart failure. Some of them are purely surgical, and some of them utilize regenerative medicine applied surgically. There are new therapies that are synergistic combinations of surgery and regenerative medicine. Combined materials could be cellular therapy, gene therapy, administration of growth factors, and tissue engineering. In this chapter, we take a general view of new but relatively familiar approaches of regenerative medicine to heart failure, and, in the final section, introduce "surgical regenerative therapy" developed in our research laboratory and clinical practice at Kyoto University.

22.2. Cellular Therapies

Cell transplantation for severe heart failure has drawn the attention of many basic and clinical researchers from the early 1990s onward. A good deal of literature was published in this field, and most of them reported promising results.[1–18] The concept of the therapies is simple: to restore lost myocardium dimensionally and/or functionally by transplantation of cells. Cell sources are broadly divided into two categories: myogenic cells and stem or precursor cells.

Despite strong expectation and rapid clinical application of this method, the exact mechanisms and optimal conditions of cellular therapies remain to be clarified. It is our future challenge that we establish these therapies as reliable treatment strategies for end-stage heart failure.

22.3. Myogenic Cells

There are three myogenic cell sources for transplantation: cardiomyocytes,[1–6] skeletal myoblasts (SMs),[7–17] and smooth muscle cells.[18] In this section, cardiomyocytes and SMs are briefly reviewed as donors for cellular therapies to treat the diseased heart.

22.3.1. Cardiomyocytes

Since the ultimate goal of cell transplantation should be the complete replacement of dead or scarred myocardium, it is natural to use cardiomyocytes as donor cells. In fact, this cell line was in use in the first experimental series of cell transplantation to the diseased heart. Since then, most of the studies about cell transplantation to the failing heart were performed with fetal or neonatal cardiomyocytes in the early 1990s. However, this cell source has high hurdles for its clinical use. The reasons were as follows.

1. Adult cardiac cells have very poor potential, if any, for proliferation. The cells should therefore be fetal or neonatal to obtain enough number of viable cells in the recipient tissue. This limitation not only has a disadvantage in availability but also raises strong ethical issues. For the same reason, cardiomyocyte transplantation should be allogeneic rather

than autologous, because the vast majority of patients with heart failure are adults.
2. Cardiomyocytes are not resistant to ischemia compared with other myogenic cells. Although the precise measurement of cell number is difficult, the ratio of viable cells among transplanted cardiomyocytes may be less than 1%.[3] In our laboratory data using a rat coronary artery ligation model, the viable tissue derived from donor cells is less than one fourth in cardiomyocyte transplantation than in SM transplantation when the same number of cells (5×10^6) is applied (unpublished data).

To solve these problems, some researchers have been seeking a way in the study of cardiac or embryonic stem (ES) cells. But some researchers lost their interest in this cell line, and moved into the study of other cell sources.

22.3.2. Skeletal Myoblasts

Menasché and colleagues reported the first human application of myoblasts performed in June of 2000, which was a landmark of this therapy.[13] At present, among myogenic cells used in cell transplantation for heart failure, SMs are the most successful and promising cells, provided that they are solely applied for transplantation. Overall, they consistently show a differentiation of implanted myoblasts into multinucleated myotubes, the lack of coupling between engrafted myotubes and host cardiomyocytes, but, nevertheless, an improvement in local and global left ventricular (LV) function.[19]

SMs, also called satellite cells, lie in a quiescent state under the basal membrane of skeletal muscle fibers. When muscle injury occurs, they rapidly repair the damaged muscular tissue by being proliferated and fused into myotubes. Considering the clinical application of the cell line, several characteristics are favorable for transplantation.

1. They can be obtained from other parts of the body (for instance, from the hip) of ill patients with little effect on the patient's hemodynamics or condition. They are of autologous origin, and therefore, do not raise ethical issues or antigenic problems. The other advantage is in the easy availability.
2. They are relatively tolerant of harsh conditions such as ischemia or enzyme-rich environment. They have a high proliferation potential in appropriate culture conditions. Therefore, expansion of the cells in vitro is relatively easy and can be conducted within 2 weeks of harvesting. Of note, rapid and steady expansion of the cells is a key factor in autologous transplantation. In addition, these characteristics are also very important in sustained viability of donor cells in the recipient tissue after transplantation.
3. The fate of SMs is to fuse into myotubes or to remain as myoblasts. Therefore, there is little chance for tumorigenicity in SM transplantation.

Although the mechanisms behind SM transplantation improving cardiac function remain unclear, a positive correlation has been demonstrated between the magnitude of improvement and the donor cell number or donor-derived muscle volume when implanted into the infarct area.[14,17] At least, elastic and passive contractile property of donor-derived structures seem to be important for dimensional and functional benefits on the recipient heart. On the other hand, some investigators reported induction of angiogenesis at the site of implantation after SM transplantation.[13] However, our study using pin-hole single photon emission computed tomography (SPECT) in a rat myocardial infarction (MI) model clearly demonstrated that the angiogenic effects of SMs are, if any, very small compared with those of basic fibroblast growth factor (bFGF).[20] It is possible that angiogenesis induced in SM transplantation may not be solely derived from transplantation.

A number of efforts have been made to avoid culture cells before transplantation. According to Menasché, experience with myoblast transplantation for the past several years suggests that the alleged disadvantages of cultures (2- to 3-week duration, risk of contamination, and cost) are largely outweighed by the advantage of injecting a well-defined, tightly controlled cell therapy product.[19]

Until now, at least six phase I trials of autologous SM transplantation have been performed, four of which were performed with coronary artery surgery while the others were designed as a catheter-based stand-alone procedure.[19,21] Consequently, the SM has entered phase II multicenter randomized

DropBooks

clinical trial (MAGIC, Myoblast Autologous Grafting in Ischemic Cardiomyopathy trial) in Europe to test efficacy. To monitor and terminate life-threatening ventricular arrhythmias, all patients will receive an implantable cardioverter defibrillator.

What has been established by all these studies so far is that autologous myoblast transplantation is technically feasible, can be implemented clinically without specific procedural complications, and results in differentiation of myoblasts into myotubes whose engraftment seems to be sustained over time. What is likely, though still unproven, is that intramyocardial skeletal muscle grafts may represent arrhythmogenic substrates. What is still uncertain is whether myoblast transplantation can restore some viability and function in scarred areas to the point that it favorably impacts on global LV function and patient outcomes.[19] Further investigation is warranted.

22.4. Stem Cells or Precursor Cells

Stem or precursor cells have the unique property of plasticity that is not provided in somatic cells. This character allows them to change their phenotype in response to still undetermined organ-specific signals. Therefore, they might differentiate along the organ-specific lineage and, thus, specifically convert into cardiac or endothelial cells after engraftment into ischemically damaged myocardial tissue.[19] In this section, bone marrow cells (BMCs), endothelial progenitor cells, cardiac progenitor cells, and ES cells are discussed.

22.4.1. Bone Marrow Cells and/or Endothelial Progenitor Cells

In 2001, Orlic and associates reported, in a mouse model, regeneration of the infarcted myocardium after injection of a specific subpopulation of progenitor cells (phenotypically defined as lin^- c-kit^+) and cytokine-induced mobilization of bone marrow stem cells. In the transplantation study,[22] cells were injected 5 h after coronary artery ligation and results were assessed 9 days later. In the mobilization study,[23] the cytokine treatment was started before the infarct and splenectomy was performed to limit systemic trapping of mobilized cells. In spite of these clinically irrelevant features, these experiments have strengthened the idea that BMCs could effectively repair infarcted myocardium. Since then, BMC transplantation has been talked up and used in humans with little preclinical data. More data are now being accumulated.[19]

So far, at least 11 trials have been published.[21] In 1999, the first angiogenic therapy using BMCs was performed in Japan. Hamano and colleagues reported that autologous BMCs were directly injected in the ungraftable ischemic territory during coronary artery bypass grafting (CABG) in five patients with ischemic heart disease.[24] One year later, myocardial perfusion scintigraphy demonstrated the improvement in myocardial blood flow at the area of transplantation in three patients, and no side effects derived from cell transplantation were observed in any patient. The earlier two studies from Germany have entailed the direct intracoronary injections of mononuclear cells[25] or endothelial progenitors derived from circulating blood or bone marrow[26] in patients with acute MI. However, in these trials, the grafted areas were also subjected to angioplasty, which makes the assessment of the respective benefits of cell therapy virtually impossible. Two surgical studies have entailed direct epicardial injections of mononuclear cells[24] or $CD133^+$ progenitor cells during coronary artery surgery.[27]

Although the mechanisms of action are not fully elucidated in transplantation of BMCs or endothelial progenitor cells, there are several hypotheses, which include transdifferentiation or fusion of donor cells to cardiomyocytes, mobilization of cardiac stem or progenitor cells, and angiogenesis.[21]

Safety remains a major concern of the procedure. Ventricular arrhythmias have not been detected in patients who have received doses of BMCs, as opposed to the SMs. However, a recent report by Kang and coworkers[28] highlighted other potential side effects of delivering BMCs to the heart.[21]

22.4.2. Cardiac Stem Cell

In 2003, Beltrami et al. reported that the c-kit^+ cells present in the heart have pluripotency and proliferative ability in vitro.[29] These cells can differentiate into not only cardiomyocytes but also smooth muscle cells and endothelial cells.[30]

Transplantation of the cells into a murine MI model confirmed their ability to differentiate into cardiomyocytes in vivo, implying the existence of a tissue repair mechanism by cardiac stem cells (CSCs) in the heart, similar to stem cells in other organs.

Throughout the myocardium, pools of CSCs may participate in the continual replacement of apoptotic cardiomyocytes at a low basal level.[31] Unlike terminally differentiated cardiac cells, CSCs are small cells that do not express cardiac markers and that can self-renew and proliferate. Several seemingly different but overlapping populations of progenitor cells (such as Sca-1-, c-Kit-, c-Met, and Abcg2-expressing side populations) can be induced to activate cardiomyocyte-specific genes in vitro. In addition, Sca-1- or c-Kit-expressing cells may differentiate into cardiomyocytes in vivo, contributing to repair of the damaged heart after acute MI, but their potential is limited, in part, by the small number of endogenous CSCs. Most of these endogenous CSCs reside in the atrioventricular groove area. Attempts to mobilize and to expand endogenous progenitor cells by introducing growth factors hold promise but remain controversial.[6] It is likely that the activity of endogenous CSCs will have to be augmented, through knowledge of the mechanisms of normal progenitor expansion and determination during embryonic development, before these cells will contribute substantially in the extreme setting of infarcted hearts. Before those cells are used in the clinical setting, the methods of mobilization and expansion of the cell line should be established.

22.4.3. Embryonic Stem Cells

The first mouse ES cell line was established by Evans in 1981, and its superior proliferative ability and pluripotency led to the establishment of a number of developmental model systems and knockout mice. In the mid-1990s, ES cell research slowly moved to using experimental animals as in vivo models for cell transplantation therapy. In 1998, human ES cells were established by Thomson et al., and although ethical issues remained, they quickly attracted significant attention as a source for regeneration therapy.

In 2001, Wakayama et al. established murine ES cells by applying nuclear transfer techniques to nuclei derived from somatic cells. These findings raised the possibility of using somatic cells from patients to produce their own ES cells and by a technique that would avoid immune rejection in humans.

In the same year, it was reported that human ES cells, like mouse ES cells, could differentiate into cardiomyocytes with cardiac-specific structural and functional properties. The same group recently revealed that transplanted human ES cell-derived cardiomyocytes can act as pacemakers in porcine ventricles in which complete atrioventricular block was artificially generated. In this study, the human ES cell–derived cardiomyocytes made successful electrical connections with the recipient cardiomyocytes in large animals.

Besides ethical issues, several problems associated with ES cells, including tumorigenicity, ectopic differentiation, and transplantation issues, need to be overcome for the clinical application of these cells.[30]

22.5. Gene Therapies

Since Losordo and colleagues reported that naked plasmid DNA encoding vascular endothelial growth factor (VEGF) (phVEGF165), which was injected directly into the ischemic myocardium, improved myocardial perfusion in patients with symptomatic myocardial ischemia,[32] a number of clinical trials of gene therapies were conducted for intractable angina from ischemic heart disease that could not be treated conventionally. The first report of a randomized, double-blind, placebo-controlled trial for ischemic heart disease was the Angiogenic Gene Therapy (AGENT) trial, in which intracoronary administration of FGF-4 was conducted in patients with chronic stable angina by using adenovirus as a vector.[33] In this trial, although anti-ischemic effects by FGF-4 were recognized, its clinical benefits were not clearly demonstrated.

Although gene therapies may be a very promising treatment tool, at least presently, several issues remain to be settled. Because we have no vectors whose activities are fully regulated, there are concerns about safety of the therapies,

DropBooks

especially for systemic side effects. In addition, for the same reason, the level and period of gene expression are hard to predict precisely.

22.6. Administration of Growth Factors

Another approach to deliver growth factors is administration of the substances in the form of peptides. Since the first trial was performed by Schumacher and associates,[34] in which acidic fibroblast growth factor was directly injected into the ischemic myocardium in ungraftable areas in patients undergoing CABG, a number of clinical trials to administer peptides were conducted in patients with ischemic heart disease. Until now, there have been no randomized, double-blind trials that have demonstrated clear beneficial effects of intracoronary or intravenous infusion of VEGF or bFGF peptides. In a clinical trial in which control-released bFGF incorporated into heparin-arginine beads were subepicardially administered, relief of anginal pain was recognized in all the patients, and significant decreases in the areas of perfusion defects were also demonstrated in dipyridamole-stress myocardial scintigraphy at 90 days after treatment in the treatment group.[35]

Large-scale clinical studies using control-released bFGF have not been performed. Based on our limited experience in basic and clinical investigation, it seems to be very important that peptides should be delivered in a controlled-release fashion with the use of some biotechnological technique.

22.7. Novel Approach—Surgical Regenerative Therapy

In this section, we introduce a novel therapeutic approach in which surgery and regenerative medicine are synergistically collaborated and combined. Some of the methods are clinically applied in the form of clinical trial at Kyoto University. We call this approach surgical regenerative therapy in order to differentiate it from other regenerative therapies using surgical techniques for their application (for instance, epicardial injection of cells or vectors). The aim of this treatment is to obtain the beneficial effects on failing hearts that cannot be achieved by surgery or by regenerative therapy alone. Synergistic effects are the key points in this novel approach.

22.8. Control-Release of Growth Factors

The functioning mechanisms of various cytokines or growth factors have been elucidated in recent years, and it is now recognized that most of the biologically active agents work in autocrine and/or paracrine fashions. The biological half-lives of such substances are usually very short (in the order of seconds or minutes). Therefore, to maintain the local concentrations higher than appropriate levels, a device or vehicle is required to deliver the agent. For this purpose, Tabata and associates developed a control-release system for various biologically active peptides using biodegradable gelatin hydrogel. In this system, peptides are incorporated into the hydrogel with electrostatic forces, and gradually released in situ along with hydrolysis of the gelatin. The characteristics of this method include the following:

1. The rate of control-release of peptides can be regulated by changing the water content in hydrogel. Usually, 2–4 weeks of control-release can be achieved.
2. The high concentrations of the peptides are limited in the local area of administration.

In our animal experiments using radioisotopes, systemic blood concentrations of control-released peptides were almost zero at 24 h after administration, and less than detectable levels at 2 days and thereafter. The gelatin hydrogel has various forms, and we usually use microspheres and sheets, which are impregnated with various growth factors.

Taken together, we consider that this method is one of the safe and effective therapeutic strategies for administration of growth factors, because it enables in situ administration of peptides almost without losing the activities or causing systemic side effects.

22.9. Arteriogenesis by bFGF—Comparison with BMC Transplantation and Other Angiogenic Factors

Before going into the topic of surgical regenerative therapy, we introduce here an interesting study conducted in our group to investigate the difference in quantity and quality of angiogenesis between control-release of bFGF and BMC transplantation using a pig MI model.

MI was created in 18 swines by transcatheter embolization of the left anterior descending (LAD) artery.[8] Four weeks later, they were randomized into three groups. Group I ($n=6$) served as control with only saline injection, Group II ($n=6$) had bone marrow–derived mononuclear cell transplantation [total $(1–2)\times10^8$ cells], and Group III ($n=6$) received injection of bFGF-impregnated gelatin hydrogel microspheres (bFGF: 200 μg). Each agent was subepicardially or intramuscularly injected at five peri-MI areas per animal. Four weeks after the treatment, LV function was estimated by an echocardiography and cardiac catheterization. Plasma levels of brain natriuretic peptide (BNP) were measured at baseline and at 4 weeks.

Before treatment, there was no significant difference in cardiac function among the three groups. Four weeks after the treatment, Groups II and III had smaller LV end-diastolic dimensions (LVEDD: 56.7 ± 6.2 vs. 49.2 ± 4.6 vs. 49.1 ± 4.9 mm, respectively, $p<0.05$), better ejection fractions (45.7 ± 9.1 vs. 62.6 ± 12.0 vs. 63.4 ± 10.1%, $p<0.05$), and better end-systolic elastance (1.34 ± 0.26 vs. 1.52 ± 0.83 vs. 1.72 ± 0.65 mmHg/ml, $p<0.01$) than Group I. There was no significant difference between Groups II and III in any parameters. The plasma levels of BNP were highest in Group I (1,394 ± 383, 1,031 ± 91, 934 ± 306 pg/ml, $p<0.05$). On microscopic examination, neovascularization was found in the peri-infarct area in Groups II and III. It should be noted that the number of vessels more than 50 μm in diameter in Group III was higher than those in Groups I and II (6.9 ± 3.9, 15.0 ± 5.2, 26.2 ± 7.1 per square meter, $p<0.05$) (Figure 22.1). In an occasional section, we found cartilage formation derived from donor BMCs.

We should be careful when interpreting these results, because we do not know what doses of bFGF are equivalent to a given dose of BMCs. However, our findings suggest a significant difference in angiogenic properties between bFGF administration and BMC transplantation. Namely, bFGF induces arteriogenesis, but BMCs does not.

Similarly, although we applied the control-release system to various growth factors such as bFGF, HGF, VEGF, and IGF-1 to expect neovascularization, bFGF may be superior for the purpose, because it is the only angiogenic factor that significantly causes arteriogenesis among them. It should be noted that the increase in collateral blood flow of the ischemic myocardium is mainly generated by arteriogenesis rather than angiogenesis at capillary levels.

22.10. Control-Released bFGF and Cardiac Surgery

Although percutaneous coronary intervention (PCI) and CABG have been widely accepted as standard treatments for ischemic heart disease, the efficacy in hearts with diffuse and severe coronary stenosis is often questionable or insufficient, because these conventional revascularization remedies cannot secure enough blood supply to the myocardium at cell levels. In this perspective, therapeutic angiogenesis for severely ischemic hearts has recently drawn increasing attention of cardiologists and cardiac surgeons. We use bFGF-impregnated gelatin hydrogel (bFGF: 200 μg) for angiogenesis and arteriogenesis.

22.10.1. Regeneration of the Sternum

Most of the cases of cardiac surgery are performed through median sternotomy. Poor or delayed healing of the sternum is one of the more troublesome complications encountered after sternotomy, especially in patients with elderly age, severe heart failure, or diabetes mellitus. Poor healing of the sternum often leads to deep sternal wound infection, which may possibly devastate surgical benefits. In this era of off-pump coronary artery bypass surgery (OPCAB), the internal mammary or thoracic arteries (IMA or ITA) are more frequently used, because they are in situ arterial grafts that have excellent patency rates. Therefore, if good healing of the sternum is guaranteed, surgeons

DropBooks

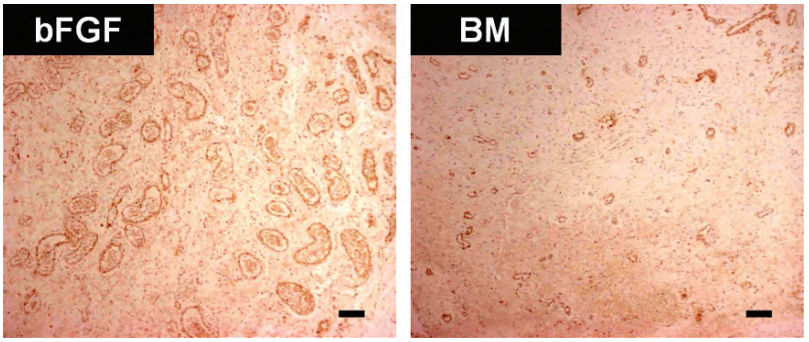


FIGURE 22.1. Neovascularization in the peri-infarct area after control-released bFGF administration (left) versus bone marrow cell (BMC) transplantation (right). A lot of large vessels with diameters over 100 μm are recognized in the bFGF group, while most of the vessels are in small diameters in the transplantation group. Scale bars represent distances of 100 μm in both panels.

would feel more comfortable using bilateral ITAs in OPCAB for high-risk patients.

With this in mind, we conducted a series of studies to place bFGF-incorporating gelatin hydrogel sheet on the ITA beds after removal of the ITAs. It was also favorable for us that bFGF also has not only angiogenic but also osteogenic activities. First, using a healthy rat model, we demonstrated that the application of the bFGF sheet offset sternal ischemia and facilitated its healing, probably because of the angiogenic and osteogenic effects of bFGF after sternotomy with BITA removal. Similar results were obtained in diabetic rats and large animals.

Following the animal studies, we started the sternum regeneration therapy with the use of bFGF-control-releasing sheet (bFGF: 200 μg) in November of 2004 at Kyoto University Hospital, and two cases have been finished until now. The first case was a female patient with coronary artery disease who underwent OPCAB using the left ITA to the LAD, and the second one was a male anginal patient who underwent on-pump coronary artery surgery with total arterial grafting using bilateral ITAs and right gastroepiploic artery (GEA). In both cases, pains on effort at the site of median sternotomy disappeared in 2 weeks after operation, no side effects were recognized, and all the grafts were patent.

22.10.2. Enhancement of Distal Runoff in Coronary Artery Surgery

In a rat coronary ligation model, when bFGF-incorporating gelatin hydrogel microspheres (bFGF: 100 μg) were intramyocardially injected into the infarct and peri-infarct areas, the treatment group showed inhibition of LV dilatation and improvement in LV systolic function. In addition, histological assessment revealed rich neovascularization in the peri-infarct area after the bFGF treatment, which was supported by the finding of improvement in the blood flow around the infarct on postoperative perfusion scintigraphy.

We conducted a similar study using a pig model in which chronic MI was created in the LAD territory. In this study, bFGF-incorporating gelatin microspheres (bFGF: 200 μg) were intramyocardially injected into the peri-infarct area. Four weeks after operation, coronary angiography demonstrated that the distal part of the ligated artery was filled via collateral vessels, and BNP levels, which is an indicator of heart failure, were significantly reduced in the treatment group. When applying this method to diffusely diseased target vessels during CABG, increase in the graft patency rate may be anticipated because control-released bFGF is expected to improve the distal runoff of the diseased coronary arteries.

22.10.3. Biological Coronary Artery Surgery—"Bio-CABG"

In a rabbit model of acute MI with the obtuse marginal artery ligated, we placed bFGF-incorporating gelatin hydrogel sheet (bFGF: 100 μg) on the infarct, and covered the sheet with the omentum containing the right GEA. Four weeks later, we recognized rich neovascularization at the site of the bFGF-omentum wrapping and the blood

flow directly going into the ligated obtuse marginal artery via collaterals from the gastroepiplic artery. Similar results were obtained in chronically ischemic hearts. (Figure 22.2) This method is very exciting among angiogenic therapies, because it creates biological anastomosis to such small arteries as considered ungraftable, and brings an extra cardiac blood source to the ischemic myocardium. In patients with ischemic cardiomyopathy, coronary arteries may be severely and diffusely stenotic, with coronary blood flow already limited at the coronary ostia. Even if extensive angiogenesis occurred in the myocardium, it would be very difficult to improve global myocardial blood flow in such patients. However, in "Bio-CABG," the new blood flow is obtained from the outside of the ischemic heart (GEA). Therefore, at least theoretically, major improvement in coronary blood flow may be expected in the hearts of patients with ischemic cardiomyopathy. In fact, in our study with a rabbit model of chronic myocardial ischemia, it was demonstrated that about the third of the local blood flow at the site where "Bio-CABG" was conducted was derived from the GEA.

In July of 2006, the first clinical trial of this novel method of angiogenesis was performed at Kyoto University Hospital. The case was a 56-year-old male patient with three-vessel disease. His cardiac anatomy had a dominant left coronary system. The stenosed LAD artery was a good graft target, while the left circumflex artery was large but diffusely stenotic, which was not thought to be a suitable target for grafting. Therefore, we put the left ITA to the LAD, and applied the novel angiogenic method to the ischemic circumflex territory of the patient. We administered 200 μg bFGF impregnated into gelatin hydrogel sheet, which was completely wrapped over by the pedicled omentum containing the GEA.

Two weeks postoperatively, local myocardial perfusion and systolic function in the circumflex territory were significantly improved, which was demonstrated by ^{201}Tl-dipyridamole stress SPECT and magnetic resonance imaging, respectively (Figure 22.3).

22.11. Future Prospects

Although over 10 years have passed since regenerative medicine emerged as a potentially promising therapeutic strategy for end-stage heart failure, no treatment has been established as standard treatment for any disease entity. For instance, in ischemic cardiomyopathy, PCI and CABG are still the mainstay of treatment, and the efficacies of newly developed angiogenic therapies are equivocal with few guidelines of indication. One of the reasons for this situation may be too much expectation that regenerative medicine could change the therapeutic paradigm for heart failure as a single-modality therapy. Taking PCI and CABG, the treatment effects cannot be sufficiently exerted without appropriate medication such as aspirin. Similarly, it may be reasonable to consider that regenerative medicine should be combined with other treatment approaches for full exertion of the beneficial effects.

DropBooks

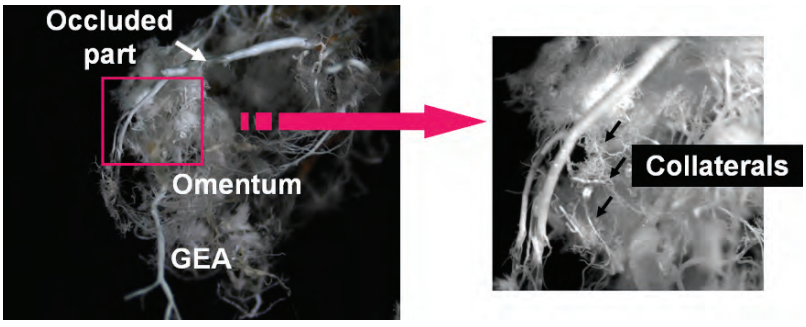


FIGURE 22.2. Microvascular corrosion cast. The pictures demonstrate collateral formation between the omentum and the occluded coronary artery. Some of the newly developed vessels have diameters over 100 μm, which, at least in part, indicates arteriogenesis. *GEA* the right gastroepiploic artery.

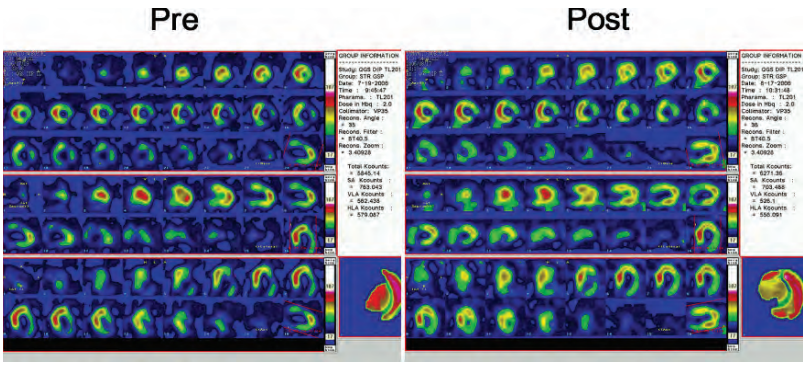


FIGURE 22.3. ^{201}Tl-dipyridamole stress single photon emission computed tomography (SPECT) before and after operation. Posterolateral areas were the target of "Bio-CABG." Significant improvement in myocardial blood flow was recognized in those areas. *Pre* the preoperative image at stress. *Post* the postoperative image at stress.

Recent developments in minimally invasive surgery are encouraging, and the minimally invasive drug delivery system using this approach may enable repetitive or serial transthoracic administration of donor cells or angiogenic factors to the heart in patients with end-stage heart failure.

For surgeons, it makes sense that we try to make the most of regenerative medicine in combination with surgery. Some of those efforts are starting to bear some fruit in the clinical setting. Before we know whether they get established as treatment options, we have to wait for the results of clinical trials, which should be ideally randomized, double-blind, placebo-controlled, multicenter studies.

22.12. Key Points to Remember

Cellular therapy remains a promise that has yet to realize its potential. While encouraging studies have suggested some improvement with injection of myocardial cells, stem cells, gene therapy, and administration of growth factors, none of them have been significant or dramatic in improving cardiac function. The ultimate role of cellular and regenerative therapy may be as an adjunct to surgery.

References

1. Li RK, Mickle DA, Weisel RD, et al. In vivo survival and function of transplanted rat cardiomyocytes. *Circ Res*. 1996;78:283-288.
2. Li RK, Jia ZQ, Weisel RD, et al. Cardiomyocyte transplantation improves heart function. *Ann Thorac Surg*. 1996;62:654-660.
3. Zhang M, Methot D, Poppa V, et al. Cardiomyocyte grafting for cardiac repair: Graft cell death and anti-death strategies. *J Moll Cell Cardiol*. 2001;33:907-921.
4. Sakakibara Y, Nishimura K, Tambara K, et al. Prevascularization with gelatin microspheres containing basic fibroblast growth factor enhances the benefits of cardiomyocyte transplantation. *J Thorac Cardiovasc Surg*. 2002;124:50-56.
5. Sakakibara Y, Tambara K, Lu F, et al. Cardiomyocyte transplantation does not reverse cardiac remodeling in rats with chronic myocardial infarction. *Ann Thorac Surg*. 2002;74:25-30.
6. Sakakibara Y, Tambara K, Lu F, et al. Combined procedure of surgical repair and cell transplantation for left ventricular aneurysm: An experimental study. *Circulation*. 2002;106(suppl I):I193-I197.
7. Chiu RCJ, Zibaitis A, Kao RL. Cellular cardiomyoplasty: Myocardial regeneration with satellite cell transplantation. *Ann Thorac Surg*. 1995;60:12-18.
8. Murry CE, Wiseman RW, Schwartz SM, et al. Skeletal myoblast transplantation for repair of myocardial necrosis. *J Clin Invest*. 1996;98:2512-2523.
9. Taylor DA, Atkins BZ, Hungspreugs P, et al. Regenerating functional myocardium: Improved performance after skeletal myoblast transplantation. *Nat Med*. 1998;4:929-933.
10. Atkins BZ, Hueman MT, Meuchel JM, et al. Myogenic cell transplantation improves in vivo regional performance in infracted rabbit myocardium. *J Heart Lung Transplant*. 1999;18;1173-1180.
11. Hutcheson KA, Atkins BZ, Hueman MT, et al. Comparison of benefits on myocardial performance

of cellular cardiomyoplasty with skeletal myoblasts and fibroblasts. *Cell Transplant*. 2000;9:359-368.
12. Reinecke H, Murry CE. Transmural replacement of myocardium after skeletal myoblast grafting into the heart: Too much of a good thing? *Cardiovasc Pathol*. 2000;9:337-344.
13. Menasché P, Hagège AA, Scorcine M, et al. Myoblast transplantation for heart failure. *Lancet*. 2001;357:279-280.
14. Pouzet B, Vilquin JT, Hagège AA, et al. Factors affecting functional outcome after autologous skeletal myoblast transplantation. *Ann Thorac Surg*. 2001;71:844-851.
15. Jain M, DerSimonian H, Brenner DA, et al. Cell therapy attenuates deleterious ventricular remodeling and improves cardiac performance after myocardial infarction. *Circulation*. 2001;103:1920-1927.
16. Pouzet B, Ghostine S, Vilquin JT, et al. Is skeletal myoblast transplantation clinically relevant in the era of angiotensin-converting enzyme inhibitors? *Circulation*. 2001;104(suppl I):I223-I228.
17. Tambara K, Sakakibara Y, Sakaguchi G, et al. Transplanted skeletal myoblasts can fully replace the infarcted myocardium when they survive in the host in large numbers. *Circulation*. 2003;108(suppl 1): II259-II263.
18. Li RK, Jia ZQ, Weisel RD, et al. Smooth muscle cell transplantation into myocardial scar tissue improves heart function. *J Mol Cell Cardiol*. 1999;31:513-522.
19. Menasché P. Cellular transplantation: Hurdles remaining before widespread clinical use. *Curr Opin Cardiol*. 2004;19:154-161.
20. Tambara K, Ohba M, Hosokawa R, et al. Effects of skeletal myoblast transplantation, BFGF administration, and the combination on tissue blood flow and left ventricular remodeling in rat infarcted hearts: Comparison using pin-hole SPECT. *Circulation*. 2004;110(17):170. Abstract.
21. Fazel S, Tang GHL, Angoulvant D, et al. Current status of cellular therapy for ischemic heart disease. *Ann Thorac Surg*. 2005;79:S2238-S2247.
22. Orlic D, Kajstura J, Chimenti S, et al. Bone marrow cells regenerate infarcted myocardium. *Nature*. 2001;410:701-705.
23. Orlic D, Kajstura J, Chimenti S, et al. Mobilized bone marrow cells repair the infarcted heart, improving function and survival. *Proc Natl Acad Sci USA*. 2001;98:10344-10349.
24. Hamano K, Nishida M, Hirata K, et al. Local implantation of autologous bone marrow cells for therapeutic angiogenesis in patients with ischemic heart disease: Clinical trial and preliminary results. *Jpn Circ J*. 2001;65:845-847.
25. Strauer BE, Brehm M, Zeus T, et al. Repair of infarcted myocardium by autologous intracoronary mononuclear bone marrow cell transplantation in humans. *Circulation*. 2002;106:1913-1918.
26. Assmus B, Schachinger V, Teupe C, et al. Transplantation of progenitor cells and regeneration enhancement in acute myocardial infarction (TOPCARE-AMI). *Circulation*. 2002;106:3009-3017.
27. Stamm C, Westphal B, Kleine HD, et al. Autologous bone-marrow stem-cell transplantation for myocardial regeneration. *Lancet*. 2003;361:45-46.
28. Kang J, Kim HS, Zhang SY, et al. Effects of intracoronary infusion of peripheral blood stem-cells mobilised with granulocyte-colony stimulating factor on left ventricular systolic function and restenosis after coronary stenting in myocardial infarction the MAGIC cell randomised clinical trial. *Lancet*. 2004;363:751-756.
29. Beltrami AP, Barlucchi L, Torella D, et al. Adult cardiac stem cells are multipotent and support myocardial regeneration. *Cell*. 2003;114:763-776.
30. Fukuda K, Yuasa S. Stem cells as a source of regenerative cardiomyocytes. *Circ Res*. 2006;98:1002-1013.
31. Srivastava D, Ivey KN. Potential of stem-cell-based therapies for heart disease. *Nature*. 2006;441:1097-1099.
32. Losordo DW, Vale PR, Symes JF, et al. Gene therapy for myocardial angiogenesis: Initial clinical results with direct myocardial injection of phVEGF165 as sole therapy for myocardial ischemia. *Circulation*. 1998;98:2800-2804.
33. Grines C, Rubanyi GM, Kleiman NS, et al. Angiogenic gene therapy with adenovirus 5 fibroblast growth factor-4 (Ad5FGF-4): A new option for the treatment of coronary artery disease. *Am J Cardiol*. 2003;92:24N-31N.
34. Schumacher B, Pecher P, von Specht BU, et al. Induction of neoangiogenesis in ischemic myocardium by human growth factors: First clinical results of a new treatment of coronary heart disease. *Circulation*. 1998;97:645-650.
35. Laham RJ, Sellke FW, Edelman ER, et al. Local perivascular delivery of basic fibroblast growth factor in patients undergoing coronary bypass surgery: Results of a phase I randomized, double-blind, placebo-controlled trial. *Circulation*. 1999;100:1865-1871.

UroPBooks

Index

Note: Page numbers followed by f indicate figures; t indicate tables

A
Abiomed BVS 5000 support system, 124–126
Abiomed Heart Booster, 191–192
Ablation therapy. *See also specific ablation techniques*.
  alternative energy sources for, 236–238
  approach options in, 239
  for atrial fibrillation, 231–234
  circumferential ablation, 232–233
  cryoablation. *See* Cryoablation.
  endocardial lesion set for, 237f, 239f
  epicardial, 228
  focal ablation, 232
  with ICDs, 226–227
  by microwave, 237
  outcomes in, 233, 240–241
  QRS complex before and after, 226f
  by radiofrequency, 236–237
  ventricular reconstruction with, 228–229
  for ventricular tachycardia, 225–229
ACC/AHA. *See* American College of Cardiology/American Heart Association (ACC/AHA).
ACE inhibitors. *See* Angiotensin-converting enzyme (ACE) inhibitors.
Acidosis, 296
Acorn Cardiovascular Corp., 57–58
Acorn CorCap cardiac support device (CSD), 32, 178, 250–251
Actuarial survival
  after rejection episode, 90f
  after transplantation, 94
Acute kidney injury (AKI)
  B.E.S.T. kidney study on, 299
  CPB and, 297–298
  dopaminergic agonists and, 300
  postoperatively, 296–297
  prevention and pharmacotherapy in, 297–299
  risk factors for, 297
Acute renal failure (ARF), 113–114
Acute tubular necrosis (ATN), 299
Adenosine triphosphate (ATP), 81, 101
Admissions (hospital), causes of, 7
Adrenaline (epinephrine), 112t, 285–286, 291
Adrenergic receptors, 51, 62–63
Age
  CHF and, 7
  as contraindication, 114
  as guideline for surgery, 42
  of heart donors, 79–80
  mitral valve replacement and, 182
Alcohol use, 80
Aldosterone, 12
Alfieri, Ottavio, 254
Alfieri stitch, 48f, 254
Algorithms
  of Berlin Group for IDCs, 63, 64f
  for surgical options, 43–44
  for timing of device support, 115f
Allografts. *See* Grafts/allografts.
Alpha-2 adrenergic agonists, 298
Alpha-2 receptor agonists, 280–282, 285–287
American College of Cardiology/American Heart Association (ACC/AHA)
  on cardiac transplantation, 33, 34f
  on heart failure therapies, 24
  on use of coronary angiography, 26
American Heart Association (AHA), on CHF incidence, 6
Amiodarone, 204, 246, 294
Amiodarone Reduction in Coronary Heart (ARCH) trial, 246
Amlodipine, 17
Amnesia, 280, 282
Amphetamines, 25t
Amrinone, 291

α-myosin heavy chain (MHC), 13
Anagrelide, 25t
Analgesia, 280, 282, 296
Anastomosis/ses
  of aorta, 82, 83f
  in coronary artery bypass, 102f, 104f, 105f, 106, 108–111
  of pulmonary artery, 82, 83f
  U-clip Spider for, 108f
  of vena cava, 82
Anemia of chronic inflammation, 302
Anesthesia Patient Safety Foundation, 220
Anesthesia/anesthetic management
  assessment of, 288
  on cardiopulmonary bypass, 280, 289, 290, 292
  challenges in HF surgery, 279, 289–301
  drugs used in, 280–282, 290–293
  general anesthesia. *See* General anesthesia.
  goals of, 280
  in hemodynamic instability, 290–293
  high thoracic epidural anesthesia, 219–221
  patient monitoring during, 280–282
  regional anesthesia, 281
Anesthesiologists
  competency for cardiac surgeries, 105–106, 280–281
  preoperative assessment by, 279–280
Anesthetics, 280–283
Aneurysmectomy, 149–150, 152f, 158f
Aneurysms
  left ventricular, 4–5, 18, 146f, 148–150
  postinfarction, 28
Angiogenesis, 308, 311–315
Angiography
  coronary, 26, 27t, 44
  pulmonary, 263–264
Angiotensin II, 12
Angiotensin-converting enzyme (ACE) inhibitors, 16–17
Annular flexibility, 168, 169f, 175f
Annuloplasty
  history of, 4, 18
  of mitral valve, 4, 49
  partial vs. complete, 178–180
  rings for, 181f
  tricuspid prophylactic, 81, 211, 218
  with undersized valve ring, 49
ANP. *See* Atrial natriuretic peptide (ANP).
Anrep effect, 78
Antero-apicoseptal location, 140, 144f, 146, 159f
Antiarrhythmic drugs, adverse effects of, 25t
Anticoagulant therapy, 118, 145, 266
Antidepressants, tricyclic, adverse effects of, 25t
Antihyperlipidemic drugs (statins), 16
Anti-inflammatory drugs, adverse effects of, 25t
Antilymphocyte globulins, 86
Antiplatelet therapy, 118
Aorta
  anastomosis of, 82, 83f
  cross-clamping of, 209, 277f
Aortic pressure tracings, 120f
Aortic stenosis, 67
Aortic valve
  insufficiency or regurgitation of, 116
  prostheses for, 116
  sternal sparing incisions for, 208–209
Apical positioning devices, 105f
Aprotinin, 117
ARCH. *See* Amiodarone Reduction in Coronary Heart (ARCH) trial.
α-receptor density, 51
ARF. *See* Acute renal failure (ARF).
Arginine vasopressin, 285–287
Arrhythmias
  ablation for. *See* Ablation therapy.
  in CHF, 15–16
  circulatory support for, 117
  postop management of, 168–170, 245–246
  transplantation for, 33t
Arteries. *See also specific arteries*.
  for allografts. *See* Grafts/allografts.
  anastomosis of. *See* Anastomosis/ses.
  for IABP conduits, 120
  regeneration of, 311–315
  transposition of, 273–275
Arteriogenesis, 311–315
Artificial heart. *See* Total artificial hearts.
Atherosclerosis, coronary, 23–24
ATP. *See* Adenosine triphosphate (ATP).
Atrial appendage, left, 235–237, 239f
Atrial fibrillation (AFib)
  paroxysmal or persistent, 232–233
  postoperatively, 245–246, 294
  surgical therapy for. *See* Ablation therapy.
  thromboembolism from, 235
Atrial natriuretic peptide (ANP), 299–300
Atrioventricular block (AVB), 246
Axillary artery, 120
Azathioprine, 85–86, 214

B

BACE. *See* Basal annuloplasty of the cardia externally (BACE).
Backward failure, 23
Barnard, Christiaan, 5
Basal annuloplasty of the cardia externally (BACE), 255–257, 258f
Basic fibroblast growth factor (bFGF), 308, 312–313
Basiliximab, 86

DropBooks

Batista procedure
defined, 28
outcomes of, 58–59
Batista, Randas, 4, 18
Beating heart surgery, technical difficulty of, 160, 203–204
Beginning and Ending Supportive Therapy for the Kidney (B.E.S.T.) study, 299
Benchmark Registry, 120, 121t
Benzodiazepines, 280–282
Berlin Group, 62–63, 64f
Berlin Incor blood pumps, 61f
B.E.S.T.. *See* Beginning and Ending Supportive Therapy for the Kidney (B.E.S.T.) study.
Beta-2 agonists, 25t
Beta-adrenoceptor blockade, 17, 245–246
Beta-receptor agonists, 285–287
Biatrial technique for transplantation, 82
BiCaval technique for transplantation, 82, 83f, 84f
Billroth, Theodor, 2
Bio-CABG. *See* Coronary artery bypass graft (CABG).
Biopsy/ies (bx), endomyocardial, 26, 87, 88t, 214
Biventricular (BiV) pacemekers, 28, 244
Bleeding/hemorrhage
assessment of, 293–294
perioperative, 117
post-transplantation, 217t
Blood gas analysis, 281–282
Blood pressure, arterial, 281–282
Blood pumps. *See* Left ventricular assist devices (LVADs).
Blood urea nitrogen (BUN), 216t
BMC. *See* Bone marrow cell (BMC) transplantation.
β-myosin heavy chain (MHC), 13
BNP. *See* Brain natriuretic peptide (BNP).
Body temperature, 281–282
Bolling, Steven, 4, 18
Bone marrow cell (BMC) transplantation, 309, 312–313
Bovine pericardial patches, 166
Bradyarrhythmias, 19, 246
Brain death, 76–78
Brain natriuretic peptide (BNP), 312
β-receptor density, 51, 62–63
Bridging, circulatory support for, 62–63, 113–134
Brockenbrough catheter, 123
Brunton, Lauder, 2–3
BUN. *See* Blood urea nitrogen (BUN).
Buxton, Brian, 110

C

Calcineurin inhibitor-based immunosuppression, 84–85, 218
Calcium, 287
Calcium channel blockers, 17, 25t
Cappelen, Ansel, 2
Carbamazepine, 25t
Carbon monoxide poisoning, 80
Cardiac Dimension device, 254
Cardiac index, 114t, 291
Cardiac magnetic resonance (CMR), 139–140
Cardiac output (CO), 290, 291f
Cardiac rejection
early efforts against, 5
endometrial biopsy grading of, 87, 88t
immunosuppression of, 84–87
survival after, 90f
Cardiac Resynchronization Therapy (CRT), 243–245
Cardiac stem cells (CSCs), 307–310
Cardiac Transplant Research Database (CTRD), 54, 79–80
Cardiectomy, 81–82
Cardioclasp ventricular restraint, 251–252
Cardiogenic shock, 113
Cardiologists, referrals to, 42
Cardiomyocytes
death of, 14, 307–308
regeneration of, 308–310
Cardiomyoplasty, dynamic, 4, 17–18, 32
Cardiopulmonary assist devices, 32
Cardiopulmonary bypass pumps
anesthesia technique and, 280
avoidance of. *See* Off-pump coronary artery bypass (OPCAB).
inflammatory response to, 106, 293
for PTE, 266
rising lactate level on, 204
use of, 103, 145–146
weaning from, 169, 204, 269
Cardiorespiratory depression, 282
Cardiovad (KCV) system, 196–198, 200
Cardiovascular accident (CVA) after CABG/OPCAB, 104
Cardiovascular drugs, adverse effects of, 25t
CardioWest total artificial heart, 55, 56f, 115t, 133–134
Carrel, Alexis, 3
Carroll, Alexis, 4
Carvedilol, 17
Cataracts, 93
Catecholamine storm, 78
Catecholamines, 285
Catheter ablation. *See* Ablation therapy.
Catheters
ablation therapy with. *See* Ablation therapy.
Brockenbrough catheter, 123
pulmonary artery catheters, 283–284
Swan-Ganz catheters, 106–107, 210
CCTGA. *See* Congenitally corrected transposition of great arteries (CCTGA).
Cell death (cardiomyocytes), 14, 307–308

Cells
angiogenic, 312–315
myogenic, 307–310
Cellular therapies, 307–315
Central venous pressure (CVP), 114t, 283
Cerebral function, 281–282
CHF. *See* Congestive heart failure (CHF).
Cholelithiasis, 93
Chordae tendonae, 48, 49f, 172, 173f, 175f
Chronic obstructive pulmonary disease (COPD). *See also* Congestive heart failure (CHF).
as LVAD contraindication, 67, 113
Chronic thromboembolic pulmonary hypertension (CTEPH), 261–262
Cilostazol, 25t
Circlage wire fixation, 204, 207–208
Circulatory arrest, induced, 266
Circulatory assist devices (CADs)
availability in UK, 41
contraindications to, 66–68
for destination therapy, 199–201
energy types in, 191
history of, 191
for lifetime, 49, 55, 65–68
models/types of, 59–64, 115t, 119–134, 192–198. *See also specific devices*.
overview of, 17, 31–32
patient selection for, 65–66
used perioperatively, 293, 295f
Circulatory support
adverse events with, 117–118
for bridging, 62–63, 113–134
indications for/contraindications to, 66–68, 113–117
timing of, 114, 115f
weaning from, 118–119
Circumferential ablation, 232–233
Circumflex marginal artery, 109f
Clenbuterol, 64–65
Clonidine, 298
CO. *See* Cardiac output (CO).
Coagulation analysis, 281–282
Coapsys device (Myocor), 254–255
Coaptation. *See* Leaflet coaptation.
Cobra-adhere unipolar radiofrequency ablation device, 237f
Cocaine abuse, 80
COCPIT. *See* Comparative Outcomes and Clinical Profiles in Transplantation (COCPIT).
Collateral circulatory formation, 310f. *See also* Arteriogenesis.
Colloids/crystalloids, 285, 292
Comorbidity in surgery decision-making, 52, 102–103
Comparative Outcomes and Clinical Profiles in Transplantation (COCPIT), 53
Comparison of Medical Therapy, Pacing, and Defibrillation in Heart Failure (COMPANION), 244
Complex ventricular reconstruction (CVR), 165–168
Computed tomography (CT scan)
high resolution helical CT, 264
of left atrium and pulmonary vein, 234f
Conduction disease, 225
Conduits. *See* Grafts/allografts.
Congenital heart disease
mortality rates in, 276–277
postop management of, 276–277
transplantation for, 33t
transposition of great arteries, 273–275
univentricular circulation, 275–276
Congenitally corrected transposition of great arteries (CCTGA), 273–275
Congestive heart failure (CHF). *See also* Heart failure (HF).
defined, 5, 23
diagnosis of, 16, 26
early surgical efforts in, 1–5
incidence and prevalence of, 6–7, 23
initiation and progression of, 11–14, 142
pathophysiology of. *See* Pathophysiology.
presenting symptoms in, 14–16
statistics on, 171
surgery for. *See* Surgical procedures.
symptoms of, 7–8, 24
systemic responses to, 12–14
treatment options in, 8, 16–19
Containment devices, 250–258
Continuous renal replacement therapy (CRRT), 294t, 301
Contractility, myocardial, 279, 283–284, 290
Cooley, Denton, 5
COPD. *See* Chronic obstructive pulmonary disease (COPD).
Coronary allograft vasculopathy, 91–92
Coronary artery atherosclerosis, 23–24
Coronary artery bypass graft (CABG)
acute kidney injury and, 296–299
with BACE procedure, 256–257
bio-CABG, 313–314
concomitant with mitral valve repair, 29–30
mortality after, 49
off pump. *See* Off-pump coronary artery bypass (OPCAB).
patient selection for, 101–103
vs. PTCA, 30–31
robotically-assisted, 109
techniques for, 102f, 104f, 105f, 106–111
totally endoscopic (TECAB), 109
vs. transplantation, 46

DropBooks

Coronary artery disease (CAD)
circulatory support for, 116–117
in donor hearts, 79
revascularization issues in, 30, 31t
Coronary sinus tensioning device, 253–254
CorSet dynamic ventricular restraint, 252
Corticosteroids
adverse effects of, 25t
for immunosuppression, 84, 214
Costs
of heart failure, 23
of sternal plating, 207
of surgical procedures, 29
Counterpulsation devices, 32, 196–198, 199f, 200, 204
Cox-Maze III, 236, 240
CPB. *See* Cardiopulmonary bypass pumps.
C-pulse heart, 198, 199f
Creatinine clearance, 298–300
CRRT. *See* Continuous renal replacement therapy (CRRT).
CRT. *See* Cardiac resynchronization therapy (CRT).
Crt. *See* Serum creatinine (Crt).
Cryoablation
as adjuvant therapy, 235
equipment for, 237, 238f
outcomes in, 237
Cryolesions, adjuvant, 235
CSC. *See* Cardiac stem cells (CSCs).
CSD. *See* Acorn CorCap cardiac support device (CSD).
CTEPH. *See* Chronic thromboembolic pulmonary hypertension (CTEPH).
Cushing response, 76–78
Cutler, Elliot, 3
CyA. *See* Cyclosporine A (CyA).
Cyanoacrylate glue, 208
Cyclosporine A (CyA)
development of, 5
for immunosuppression, 84–85, 214
infection predisposition from, 90
Cytokines, systemic responses to, 12–13
Cytolytic therapy, 214
Cytomegalovirus (CMV), post-transplantation, 90–92

D

Da Vinci “robot,” 109
Daclizumab, 86
Dacron patches, 146–148, 165, 167f, 168–170
DCM. *See* Dilated cardiomyopathy (DCM).
DeBakey LVAD, 115t, 133
Deep vein thrombosis (DVT) with CHF, 16
Defibrillators. *See* Implantable cardiac defibrillators (ICDs).
Dehiscence of sternum, 207
Destination Evaluation Long-term Assist (DELTA), 199
Destination therapy, 199–203
DeVega tricuspid valve annuloplasty
management and assessment of, 214
overview of, 213
pros and cons of, 216–219
statistics and results in, 214–216
technique for, 213–214
Devices. *See specific devices*.
Diabetes medications, adverse effects of, 25t
Diagnostic imaging. *See also specific modalities*.
for heart failure, 16, 26
for myocardial ability, 102
for surgery assessment, 44, 46
Diastolic dysfunction
assisted, 197f
defined, 12
manifestations of, 45
after reconstruction, 154, 158f
Digitalis, 286
Digoxin, 16
Dilated cardiomyopathy (DCM)
defined, 11
ischemic vs. nonischemic, 174, 176f, 177f
mechanical inhibition for, 32
mitral regurgitation in, 171, 176
transplantation for. *See* Transplantation, heart.
ventriculectomy for, 28
Dilation/dilatation, cardiac
appearance of, 166f
constrainment of, 19
inhibition of, 32, 313
progression after MI, 139–142
Direct mechanical ventricular actuation (DMVA), 192
Disability classifications, 14–15, 24t
Diuretics/diuresis, 298–299
Diverticular disease, 93
DMVA. *See* Direct mechanical ventricular actuation (DMVA).
Dobutamine, 114t, 285, 291
Dobutamine stress echocardiography, 102
Domino procedure, 80
Donor organs
from brain dead donors, 76–78
CAD in, 79
procurement procedure for, 81–82
shortage of, 18, 41, 53, 76
Donor-recipient size matching, 80, 209
Donor-specific alloreacitivty, 80
Dopamine, 114t, 285, 291, 294
Dopaminergic agonists, 300
Dopexamine, 285–286, 291
Dor procedure
complications of, 167
defined, 28, 47

Dor procedure (*Continued*)
failure mode of, 168–170
goals of, 47
LV function after, 51–52
modifications of, 165–167
D'Or, Vincent, 4–5, 18
Drug therapy. *See also specific drugs and drug categories*.
adverse effects of, 25t
for CHF, 16–17
commonly used during anesthesia, 280–282, 285t
for premedication, 281
D-transposition of great arteries (D-TGA), 273–275
Duran rings, 181f
Dynamic cardiomyoplasty, 4
Dyskinesis/akinesis
myocardial, 4–5, 140–145, 151f
postoperatively, 170
septal, 5, 140–145, 151f, 167
Dyspnea, 258

E

EBV. *See* Epstein-Barr virus.
Echocardiogram/graphy (ECHO)
during ablation therapy, 232, 233f
after Alfieri stitch, 48f
vs. CVP lines, 284
dobutamine stress echo, 46, 102
indications for, 26, 44
of pre and post PTE, 263f
for TR, 214–215
transesophageal (TEE), 106–107, 284
ECMO. *See* Extracorporeal membrane oxygenation (ECMO).
Edema
cardiopulmonary in LCOS, 292
clinical presentation of, 7–8
from reperfusion, 270
Eisenmenger's syndrome, 261, 263
Ejection fraction. *See* Left ventricular ejection fraction (LVEF).
Electrocardiograph/graphy
in hemodynamic instability assessment, 283
QRS complex before and after ablation, 226f
in right heart failure, 263
Electrolytes
perioperative management of, 287, 294
role in transplantation, 81
Electromechanical mapping (EMM) system, 52
Embolisms. *See* Thromboembolic events.
Embryonic growth factors and ventricular remodeling, 12, 310–311
Embryonic stem (ES) cells, 307–310
Enalapril, 16–17
Endarterectomy, pulmonary, 265–270
Endomyocardial biopsy, 26, 87, 88t, 214
Endothelial progenitor cells, 309
Endotracheal intubation, 282
Endoventricular circular patch plasty (EVCPP), 28
Enoximone, 291
Epidural hematomas, 220–222
Epidural space
anesthesia through, 220–222
puncture pressure in, 221f
Epinephrine (adrenaline), 114t, 285–286, 291
Epstein-Barr virus (EBV), 90
Ergot alkaloids, 25t
ES. *See* Embryonic stem (ES) cells.
Ethical issues, 307–308, 310
EVCPP. *See* Endoventricular circular patch plasty (EVCPP).
Event-free survival in transplantation, 73f
Everolimus, 87
Exercise testing, 26
Exercise training programs, 16, 19
External cardiac restraint/containment, 57–58, 160
Extracorporeal circulation, 103–106
Extracorporeal membrane oxygenation (ECMO)
for bridging, 115t, 121–123
for hemodynamic instability, 293, 295f
in pediatrics, 276–277

F

Failure modes, 168–170
Femoral artery, 120, 124f, 208–209
Femoral vein, 124f, 208–209
Fenoldopam mesylate, 300
Finger fracture technique, 3
Fluid management, 292, 302
Focal ablation, 232
Fontan procedure, 275
Fontan stitch, 165
Forward failure, 23
Frank-Starling mechanism, 1–2, 77f, 249
Furosemide, 298–299

G

Gadolinium late enhancement (GLE), 140–145, 144f
Gancyclovir, 91
Gastroepiploic artery (GEA), 313–314
Gender and CHF, 7
Gene therapies, 310–311
General anesthesia. *See also* Anesthesia/anesthetic management.
defined, 281
emergence from, 282–283
induction and maintenance of, 282
supplies and equipment for, 282

DropBooks

Genes/genetics, role in CHF, 13–14
GeoFoam Rings, 181f, 182–184
Geometric mitral valve repair, 171, 178–179
Glaucoma, 93
GLE. *See* Gadolinium late enhancement (GLE).
Glenn cavo-pulmonary connection (Glenn shunt), 271
Goretex patches, 168
Grafts/allografts
  choice of, 106–111, 313–314
  cumulative patency of, 110
  dysfunction of, 213
  failure of, defined, 79
  "jump" grafts, 111f
  rejection/infection of, 87–91
  vasculopathy of, 91–92
Growth factors, 310–311

H
Harken, Dwight, 3, 4f
Heart
  beating heart surgery, 160
  cardioplegic arrest of, 203
  fibrous skeleton of, 172, 173f, 175f
  manipulation/displacement of, 107
  stabilization of, 107–108
  total artificial heart, 32, 55, 56f, 115t, 133–134, 295f
  transplantation of. *See* Transplantation, heart.
Heart failure (HF). *See also* Congestive heart failure (CHF).
  acute or chronic, 15
  arrhythmias of. *See* Arrhythmias.
  care components of, 289
  congenital, 273–277
  costs of, 23
  defined, 23
  etiology of, 6t, 23–24
  evolutionary stages of, 25t
  incidence and prevalence of, 23
  long term management of, 199f
  new therapies in, 307–315
  pathophysiology of. *See* Pathophysiology.
  pediatric. *See* Pediatric heart failure.
  prevention of, 249
  right-sided, 67, 117–118, 169, 200
  stage D (NYHA class IV), 41–42
  surgery for. *See* Surgical procedures.
  symptoms and diagnosis of, 24, 26
  treatment options in, 42–43
Heart Failure Survival Score (HFSS), 53, 66, 72
Heart sounds
  in CHF, 15
  in pulmonary hypertension, 262
Heart String, 108
HeartMate II LVAD, 115t, 131–133, 195
HeartMate XVE LVAD, 115t, 128–130, 193–194, 197f, 199
Hematologic medications, adverse effects of, 25t
Hematomas, epidural, 220–222
Hemodynamic instability
  determination and causes of, 283
  drugs for, 290–293
  mechanical support for, 293
Hemodynamics
  anesthesiologist management of. *See* Anesthesia/anesthetic management.
  management flow chart for, 295f
  post-transplantation, 83, 214–215, 216t
  of tissue perfusion, 113, 114t
  during weaning trials, 118–119, 269
Heparin, 118, 266
Hepatitis C, 80
HF. *See* Heart failure (HF).
High thoracic epidural anesthesia (HTEA)
  advantages of, 219–220
  neuroaxial trauma and, 220–222
  outcomes in, 220–221
History and physical examination, 26
Hospitals, length of stays in, 104, 301–302
HTEA. *See* High thoracic epidural anesthesia (HTEA).
Hydralazine-isosorbide combination, 17
Hydrogel biodegradable gelatin, 311, 313–314
Hyperglycemia/hypoglycemia, postoperatively, 296
Hypertension, ventricular dysfunction and, 42
Hypotension, postoperatively, 293

I
IABPs. *See* Intra-aortic balloon pumps (IABPs).
Ibutilide, 25t
ICDs. *See* Implantable cardiac defibrillators (ICDs).
ICU. *See* Intensive care unit (ICU).
Idiopathic dilated cardiomyopathy (DCM). *See* Dilated cardiomyopathy (DCM).
IL-2 receptor inhibition (anti-CD25), 86
Iliac artery, 120
Immune response, 220
Immunocompromised hosts, 89–90
Immunosuppressive therapy
  history of, 8
  infection after, 89–91
  modalities for, 84–87
Impella Recover® system, 115t, 124–125
Implantable cardiac defibrillators (ICDs)
  ablation therapy with, 226–227
  indications/contraindications for, 243
  vs. surgery, 229
  tricuspid valve and, 210–212
In vitro cell studies, 307–310
India, 106

Infants
Berlin Excor device in, 64f
LVADs for, 62f, 64f
ventriculectomy in, 59f
Infarct restraint/constraint, 252–253
Infection/s
agent categories of, 91f
around LVAD drivelines, 66f
CyA predisposition to, 90
nosocomial, 118, 301–302
perioperative prevention of, 296
post-transplantation, 89–91
Inflammation
from anesthesia modality, 220
from cardiopulmonary bypass, 106, 293
Inhaled anesthetics, 280–282
Inotropic agents
for LCOS, 290–291, 295f
studies on, 16
used during anesthesia, 285–287
Intensive care unit (ICU), 289, 291, 301
Internal mammary artery, left (LIMA)
anastomosed to circumflex, 109f
anastomosed to LAD, 102f, 104f, 105f, 106
cumulative patency of, 110
Internal mammary artery, right (RIMA), 106, 109f
Internal thoracic artery, left (LITA), 108–110, 313–314
International Society for Heart and Lung Transplantation (ISHLT)
on endometrial biopsy grading, 87, 88t
on postop mortality rates, 33
Intra-aortic balloon pumps (IABPs)
for bridging, 115t, 119–121
complications from, 120
defined, 32
for hemodynamic instability, 293, 295f
implantable, 196–198
placed preoperatively, 106–107, 169
for right-sided HF, 204
used postoperatively, 99
weaning from, 120
Intracardiac shunts, circulatory support for, 117
Investigations. *See* Diagnostic imaging; Laboratory evaluations.
Ischemia
of limb or leg, 120–121
perioperative, 116
regurgitation-related, 29–30
sternal, 312–313
Ischemic heart disease/cardiomyopathy
defined, 23–24
mechanism of, 159f
mechanisms of, 44
Ischemic time, 79
Isoproterenol, 286

J
Jarvik 2000 LVAD, 115t, 133, 195
Jarvik Flowmaker, 60, 61f, 62f
Jugular venous pulse (JVP), 15, 262
“Jump” grafts, 111f

K
Kantrowitz CardioVAD system, 196–198, 200
KCV. *See* Kantrowitz CardioVAD system.
Kidneys
CHF effects on, 12
injury to. *See* Acute kidney injury (AKI).
Kimo study, 220
Kyoto University Hospital, 307–314

L
Laboratory evaluations, 26
Lactate levels, 204
LaPlace Law, 26, 28, 44, 142, 249
Larrey, Dominique, 2
Latissimus dorsi muscle, 4, 17–18
LCOS. *See* Low cardiac output state (LCOS).
Leaflet coaptation, 172, 174–177, 179f, 210–212
Left anterior descending (LAD) coronary artery
angiogenic grafting method to, 313–314
bypass grafting of, 102f, 104f, 105f, 106–111
recanalization and stenting of, 159f
Left ventricle
aneurysms of, 146f, 148–149
containment of, 249–251
dilation mechanism in, 47
dysfunction of, 44–45
after MI, 140–142
original shape of, 163, 169, 249
reconstruction of. *See* Reconstruction, left ventricular (LVR).
restoration of, 51–52
shape change of, 251–252
volume of, 142, 185f
Left ventricular aneurysm repair, 18
Left ventricular assist devices (LVADs). *See also* Circulatory assist devices (CADs).
adverse events with, 193t
availability in UK, 41
as bridge-to-transplant, 62–63
considerations in, 114–116
contraindications to, 66–68
defined, 17, 32
as destination therapy, 199–201
explantation of, 63
indications for, 55, 116–117
for infants, 62f, 64f
infections with, 66f
for lifetime, 49, 55
models/types of, 59–64, 115t, 124–133, 192–198

PropBooks

mortality and, 65–66
PFTs and, 67
as primary treatment option, 65–68
Left ventricular dysfunction, mortality and, 44–45
Left ventricular ejection fraction (LVEF)
with Acorn CorCap device, 32, 247
after Dor procedure, 28
mortality and, 42, 44–45
outcomes and, 103
procedure-specific results for, 44–52, 56, 58, 63
after reconstruction, 149t
restoration surgery and, 47
Left ventricular end-diastolic diameter (LVEDD), 62–63
Left ventricular end-diastolic volume index (LVEDVI), 142, 251
Left ventricular end-systolic volume index (LVESVI), 46, 142, 251
Leg ischemia, 120–121
Leukocyte (WBC) immunosuppression, 84–87
Liem Group study, 219–220
LIMA. *See* Internal mammary artery, left (LIMA).
LITA. *See* Internal thoracic artery, left (LITA).
Low cardiac output state (LCOS), 290–291, 295f
Low-dose dobutamine stress echocardiography, 46
Lung ventilation-perfusion scans, 263
LV end-diastolic pressure (LVEDP), 45
LVAS. *See* Left ventricular assist devices (LVADs).
LVEDD. *See* Left ventricular end-diastolic diameter (LVEDD).
LVEF. *See* Left ventricular ejection fraction (LVEF).
LVESVI. *See* Left ventricular end-systolic volume index (LVESVI).
LVR. *See* Reconstruction, left ventricular (LVR).

M

MAGIC. *See* Myoblast Autologous Grafting in Ischemic Cardiomyopathy (MAGIC) trial.
Magnesium supplementation, prophylactic, 287, 294
Magnetic resonance imaging (MRI)
cardiac. *See* Cardiac magnetic resonance (CMR).
contrast-enhanced, 46
indications for, 44
Malignancy, after transplantation, 92–93
Manubrium, 206, 208
MAP. *See* Mean arterial blood pressure (MAP).
Mapping systems/techniques, 227–228, 232
MAV. *See* Mechanical auxiliary ventricle (MAV).
Maximal oxygen uptake (VO_{2max}), 26
Maze procedures
history of, 235
maze III, 235–236
partial vs. complete, 236
percutaneous endocardial maze, 231
McCarthy, Patrick, 5, 18, 165
Mean arterial blood pressure (MAP), 292, 295f
Mean pulmonary artery pressure, 114t, 145, 204, 262
MECA. *See* Multiple electrode catheter ablation (MECA).
Mechanical assist devices. *See* Circulatory assist devices.
Mechanical auxiliary ventricle (MAV), 196
Mediastinitis
prevention of, 204–205
risk factors in, 205
sternal plating against, 206–208
Medtronic Cardioblate, 237f
Medtronic Octopus, 105f, 108
Mental status, 283
Metformin, 25t
Methylene blue, 285–287
MI. *See* Myocardial infarction (MI).
Micromed DeBakey blood pumps, 61f, 195–196, 199
Microvascular corrosion cast, 314f
Microwave ablation, 237
Midazolam, 302
Milrinone, 101, 114t, 204, 291
Mini-thoracotomy, 208–209, 210f
Minoxidil, 25t
Mitral regurgitation (MR)
acute vs. chronic, 173–174
assessment of, 145
BACE procedure for, 255–257, 259f
with circulatory support, 116
mechanism of, 56f, 174f
new treatments in, 253–258
pathophysiology of, 29–30, 173–174
postoperatively, 166
quantification of, 146
valvular vs. geometric, 174–178
Mitral stenosis, 67, 116
Mitral valve
annuloplasty of. *See under* Annuloplasty.
in Batista procedure, 28
indications for repair, 47–49
insufficiency of, 146
mortality after repair, 55, 56, 57t
regurgitation through. *See* Mitral regurgitation (MR).
repair of. *See* Mitral valve repair.
sternal sparing incisions for, 208–209
structure and function of, 172
in systole and diastole, 173f
Mitral valve repair
anatomy and physiology of, 171–178
defined, 47–49
geometric, 171, 178–179
innovative options in, 185
patient selection for, 184–185
studies on, 179–180
timing of, 176
unresolved issues in, 181–184

Mitral valve replacement (MVR)
age and, 182
history of, 178
with mechanical prosthetic valve, 182f
with porcine bioprosthetic valve, 183f
vs. repair, 180, 182
Mixed venous oxygen content on exercise (MVo_2), 44
MMF. *See* Mycophenylate mofetil (MMF).
Monitored anesthesia care, 280
Morbidity
with circulatory support, 117–118
post-transplantation, 216t, 217t
Mortality rates
after CABG, 49–50
in congenital heart disease, 276–277
in Dor procedure, 166
with LV dysfunction, 44–45
after LV reconstruction, 148–150
with LVADs, 65–66
LVEF and, 42, 44–45
after MV repair, 55, 56, 57t
post-transplantation, 33, 216, 217t
Moulopolous, S.D., 119
MR. *See* Mitral regurgitation (MR).
Multiple electrode catheter ablation (MECA), 231
Multiple organ failure, 291
Muromonab-CO3, 86
Muscle relaxants, 280, 282
MVo_2. *See* Mixed venous oxygen content on exercise (MVo_2).
Mycophenylate mofetil (MMF), 86
Myobifrillar degeneration, 77f, 78
Myoblast Autologous Grafting in Ischemic Cardiomyopathy (MAGIC) trial, 308–309
Myoblasts, skeletal, 307–309
Myocardial infarction (MI)
antero-apicoseptal location of, 140, 144f, 146
infarct restraint/constraint, 252–253
ventricular remodeling after, 12, 42, 140–142
Myocardium
abnormal loads on, 11
contractility of, 279, 283–284
damage to, 11–12
hibernation of, 45–46, 102
necrotic, 140–145, 144f, 307–308
postreconstruction morphology and performance of, 149–150
preservation during transplantation, 80–81
repair of, 17–18
scarring of, 45, 47, 102, 140–145
stunning of, 50–51
viability evidence in, 102–103
Myocor myosplint ventricular restraint, 247, 252f
Myocytes
loss of, 46
LVAD changes in, 60
Myogenic cells, 307–310
Myotubes, 308–309

N

National Institute for Clinical Excellence (UK) on HF surgery, 42
N-Contact cryoablation probe, 234f
Necrosis, myocardial, 144f, 307–308
Neovascularization, 313–314
Nephrotoxicity, 84–85, 93, 298–300
Neuroaxial trauma, 220–222
Neurohormones
response to reconstruction, 159f
systemic responses to, 12–13
Neurologic and psychiatric medications, adverse effects of, 25t
Neuromuscular blockade
epidural, 219–221
polyneuropathy and, 302
in regional anesthesia, 301
New York Heart Association (NYHA)
class IV/stage D classification of, 41–42
functional disability classification of, 24t
HF classification of, 17–18
SOB classification of, 14–15
Nitric oxide, 12–13, 204
Nonsteroidal anti-inflammatory drugs (NSAIDs), adverse effects of, 25t
Norepinephrine (noradrenaline), 293
action of, 287
postop renal function and, 294f
systemic responses to, 13
Norwood procedure, 275
Nosocomial infections, 118, 301–302
Novacor II LVAD, 194
Novacor LVAD, 115t, 130, 194
NSAIDs. *See* Nonsteroidal anti-inflammatory drugs (NSAIDS).
Nuclear medicine tests, 46

O

Octopus (Medtronic), 108
Octopus (Medtronic) device, 105f
Off-pump coronary artery bypass (OPCAB)
acute kidney injury and, 298
anesthesiologists for, 105–106
contraindications to, 105f
vs. conventional CABG, 103–106
decision making philosophy for, 107
efficacy and safety of, 110
robotically-assisted, 109

DropBooks

sternal healing and, 313–314
techniques for, 106–111
OHT. *See* Transplantation, heart.
OKT3 (muromonab-CO3), 86
Operative mortality. *See* Mortality rates.
Opioids, 280–282
Optimal medical management (OMM), 193, 199f
Organ donation
age of donors, 79–80
in brain death, 76–78
donor evaluation in, 76, 78–79
procurement procedure for, 81–82
recipient-donor demographics of, 215t
shortage of, 18, 41, 53, 76
Orthotopic heart transplantation (OHT). *See* Transplantation, heart.
Osteosynthesis, plate, 204–208
Oxygen (O_2) measurement, 26

P

Pacemakers
biventricular (BiV), 28, 244
lead-related regurgitation, 209–212
Pacing/pacemaker implantation
biventricular (BiV), 28, 244
indications for, 19, 28
during OPCAB, 107
PAD. *See* Percutaneous access device (PAD).
Pain relief (analgesia), 280, 282, 296
Pancreatitis, 93
Papillary muscle, 172, 173f, 175f, 178
Paracor dynamic ventricular restraint, 252
Paralysis, induced, 280
PARP (poly ADP-ribose polymerase), 14
Partial left ventriculectomy (Batista procedure), 18
Patch reconstruction
alternatives for, 158–160
by Dor procedure. *See* Dor procedure.
history of, 139–140
outcomes in, 148–158
preop for, 145–148
techniques for, 140f, 142–145
Patches, myocardial
appearance of, 166f, 167f
autologous, 146, 148f
Dacron patches, 146–148, 168–170
defined, 5
Pathophysiology
of backward vs. forward heart failure, 23, 26–27
of brain death, 77f
in initiation and progression of HF, 11–14
of MR, 29–30, 173–174
Pediatric heart failure. *See also* Infants.
chronic, 275
overview of, 273
postoperatively, 276–277
surgical management of, 273–275
Peptic ulcer disease, 93
Percutaneous access device (PAD), 196–198
Percutaneous endocardial maze procedure, 231
Percutaneous transluminal coronary angioplasty (PTCA) vs. CABG, 30–31
Pergolide, 25t
Phenylephrine, 287
Phosphodiesterase inhibitors, 101, 106–107, 285–287
Photopheresis, 87
Physiologic goals of therapy, 284–285
Plaque formation, 268f
Plasmapheresis, 87
Plating systems, 204–208
Plication of septum, 163, 164f, 165, 170
Poly ADP-ribose polymerase (PARP), 14
Polyneuropathy of critical illness, 302
Positioners and stabilizers, 107–108
Positron emission tomography (PET) scan for ventricular function, 46, 102
Postoperative care, 290–294. *See also* Anesthesia/anesthetic management.
Posttransplant lymphoproliferative disease (PTLD), 93
Potassium, 294
PRAISE trial. *See* Prospective Randomized Amlodipine Survival Evaluation (PRAISE) trial.
Precursor cells. *See* Stem cell therapy.
Preload/afterload, 279, 283–284
Premedication, 281
Preoperative care, 289–290. *See also* Anesthesia/anesthetic management.
Preservation solutions, 81
Procainamide, 228
Progenitor cells. *See* Stem cell therapy.
PROMISE trial. *See* Prospective Randomized Milrinone Survival Evaluation (PROMISE) trial.
Prophylaxis
against infection, 91
magnesium supplementation for, 287, 294
against nephropathy, 298–300
tricuspid annuloplasty as, 81, 211, 218
Prospective Randomized Amlodipine Survival Evaluation (PRAISE) trial, 17
Prospective Randomized Milrinone Survival Evaluation (PROMISE) trial, 16
Prostheses for mitral valves, 182f, 183f
Proteins, regulatory contractile, 14
PTCA. *See* Percutaneous transluminal coronary angioplasty (PTCA).
PTE. *See* Pulmonary thromboendarterectomy (PTE).
PTLD. *See* Posttransplant lymphoproliferative disease (PTLD).

Pulmonary angiography, 263–264
Pulmonary artery
  anastomosis of, 82, 83f
  mean pulmonary artery pressure, 114t, 145, 204, 262
  occlusions in, 267–268
  surgical exposure of, 266–267
Pulmonary artery catheters
  vs. echocardiography data, 284
  used during anesthesia, 283–284
Pulmonary artery occlusion pressures (PAOP), 292
Pulmonary function during anesthesia, 281–282
Pulmonary function tests (PFTs), 67
Pulmonary hypertension, 261–262
Pulmonary thromboendarterectomy (PTE)
  indications for, 265
  outcomes in, 269–270
  overview of, 261–262
  presentation and diagnosis for, 262–264
  surgical technique for, 265–269
Pulmonary veins
  anastomosis of, 82, 83f
  bilateral isolation of, 237f, 239f
Pulsatile flow devices
  extracorporeal, 115t, 125–128
  implantable, 115t, 128–130
Purse-string sutures, 147f, 165, 166f

R
Radial artery, 110, 111f
Radial Artery Patency and Cumulative Outcomes (RAPCO), 110
Radiofrequency ablation, 236–237, 240
Randomized Efficacy Study of Tirofiban for Outcomes and REstenosis (RESTORE) trial, 28–29
Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH)
  HeartMate XVE in, 193–194
  on “lifetime” assistance, 49
  on LVADs, 55, 65–66
Randomized Evaluation of the Novacor LVAS in a Nontransplant Population (RELIANT), 194, 199
Reconstruction, geometric mitral, 171, 178–179
Reconstruction, left ventricular (LVR)
  complex (CVR), 165–168
  defined, 4–5
  by Dor procedure. *See* Dor procedure.
  neurohormone response to, 159f
  by patching. *See* Patch reconstruction.
  by purse-string suture, 147f, 165, 166f
  surgical options for, 28–29
  by ventriculectomy. *See* Ventriculectomy.
Recover LD 5.0 device, 124
Recover LP 5.0LV device, 124
Regenerative therapy, 311–315
Regional anesthesia, 281
Regurgitation. *See also specific valves*.
  with circulatory support, 116
  pacer- or defibrillator-related, 209–212
Rehn, Ludwig, 2
Rejection. *See* Cardiac rejection.
RELIANT. *See* Randomized Evaluation of the Novacor LVAS in a Nontransplant Population (RELIANT).
REMATCH. *See* Randomized Evaluation of Mechanical Assistance for the Treatment of Congestive Heart Failure (REMATCH).
Remodeling, ventricular
  arrest of, 103
  assessment of, 157t
  components of, 45
  defined, 12
  growth factors and, 12, 310–311
  after MI, 12, 42, 140–142
  process of, 23–24
  prognoses with, 27–29
  after reconstruction, 150–157, 158f
  reversibility of, 149–150, 152f, 158f
Renal failure, acute (ARF), 113–114
Renal function
  acute kidney injury, 296–297
  during anesthesia, 281–282
  CHF effects on, 12
  post-transplantation, 215–216, 218
  with and without norepinephrine, 294
Renal insufficiency, 67
Renal replacement therapy (RRT), 300–301
Renin-angiotensin axis, 12–13
Reperfusion edema, 270
Respiratory system, ECMO support for, 123
RESTORE trial. *See* Randomized Efficacy Study of Tirofiban for Outcomes and REstenosis (RESTORE) trial.
Resynchronization therapy, 28, 243–245
Retransplantation, 75–76
Revascularization. *See also specific modalities*.
  adjunct therapies for, 160
  issues in, 30, 31t
  timeliness of, 46
Right ventricle, 249
Right ventricle, shape of, 249
Right ventricular assist devices (RVADs), 67, 196
Right-sided circulatory failure, 67, 117–118, 169, 200, 204, 269–271, 274–275
Romero, Francisco, 2
Rotary pumps, extracorporeal
  with axial flow design, 115t, 124–125
  with centrifugal flow deasign, 123–124

DropBooks

with centrifugal flow design, 115t
Rotary pumps, implantable with axial flow design, 115t, 131–132
RRT. *See* Renal replacement therapy (RRT).

S
Saline-irrigated cooled tip radiofrequency ablation (SICTRA), 240
SAM. *See* Systolic anterior motion (SAM).
Saphenous vein
anastomosis of, 108
cumulative patency of, 110
as graft choice, 106
Sarcomeres, 13
Sarcoplasmic reticulum Ca^{2+}ATPase, 13–14
Satellite cells, 307–309
SAVE trial. *See* Survival and Ventricular Enlargement (SAVE) trial.
SAVER. *See* Surgical anterior ventricular endocardial restoration (SAVER).
Scarring, myocardial
ablation therapy with, 227–228
appearance of, 164f, 165
mechanism of, 45, 47, 102, 140
patch reconstruction for. *See* Patch reconstruction.
of septum, 157f, 161f
Scintigraphy, 102
Segmental ostial catheter ablation (SOCA), 232
Septum (heart)
affected in MI, 140
plication of, 165, 166f, 167, 170
scarring of, 157f, 161f
Serine protease inhibitor, 117
Serum creatinine (Crt), 216t, 218, 294f, 296–299
Serum markers, 63
Shape change, 251–252
Shortness of breath (SOB) NYHA classification, 14–15
Shumway, Norman, 5
Shushruta Samhita (Sushruta), 1
SICTRA. *See* Saline-irrigated cooled tip radiofrequency ablation (SICTRA).
Simplicit bands, 181f
Simvastatin, 16
Single-photon emission computed tomography (SPECT), 46, 315f
Sinus node dysfunction, 246
Sirolimus, 86–87
Skeletal myoblasts (SMs), 307–309
Smooth muscle cells, 307
SOCA. *See* Segmental ostial catheter ablation (SOCA).
SOLVD trial. *See* Studies of Left Ventricular Dysfunction (SOLVD) trial.
Sototol, 25t
Souttar, Henry, 3
Specimens, surgical (plaque), 268f
St. Jude Tailor rings, 210–211
Starling Law, 142
Statins. *See* Antihyperlipidemic drugs (statins).
Stem cell therapy, 52, 307–310
Stents/stenting, 163f
Sternal plating
indications for, 204, 208
outcomes in, 206–207
overview of, 204–205
patients and techniques for, 205–206
pros and cons of, 207–208
Sternalock system, 205–207
Sternotomy
avoidance of, 46
complications of, 208, 312–313
sternal plating for, 205–207
Sternum
dehiscence of, 207
healing of, 313–314
plating of, 205–207
regeneration of, 312–313
wire fixation of, 205–208
Steroids. *See* Corticosteroids.
STICH. *See* Surgical Trial in Intracerebral Hemorrhage (STICH) trial.
Stress testing, 26
Structural congenital defects, 274–275
Studies of Left Ventricular Dysfunction (SOLVD) trial, 17
Stunned myocardium/stunning, 45, 50–51
Sudden Cardiac Death in Heart Failure trial (SCD-HeFT), 243
Sudden death, prevention of, 243
Superior vena cava, 266–267, 277f
Surgical anterior ventricular endocardial restoration (SAVER), 28
Surgical procedures. *See also specific procedures*.
assessment algorithm for, 43–44
costs of, 29
history in heart failure, 1–5
overview of, 17–18, 27–33
treatment algorithm for, 34f
Surgical regenerative therapy, 311–315
Surgical Trial in Intracerebral Hemorrhage (STICH) trial, 169
Surgifrost-Cryoprobe, 238f
Survival and Ventricular Enlargement (SAVE) trial, 17
Survival benefit margin, 53–54, 71, 72f
Swan-Ganz catheters, 106–107, 214
Symptoms, presenting, 7–8, 24, 26
Syncope/presyncope, 258
Systolic anterior motion (SAM), 49, 178

Systolic dysfunction
assisted, 197f
defined, 26
etiology of, 42
after reconstruction, 150, 158f

T
Tachycardia, postop ventricular, 168, 246
Tacrolimus, 85
TandemHeart Percutaneous Ventricular Assist Device (pVAD), 115t, 123–124
Target of rapamycin (TOR) inhibitors, 86–87
T-cell activation, 84, 85f
TECAB. *See* Totally endoscopic coronary artery bypass (TECAB).
Technetium-99m perfusion tracing, 46
TEE. *See* Transesophageal echocardiogram (TEE).
Teflon pledgets, 146, 147f, 166f
Temperature, body, 281–282
Terumo LVAS blood pumps, 61f
TGA. *See* Transposition of great arteries (TGA).
Thallium-201 scintigraphy, 102
Thallium-210 perfusion tracing, 46
The Artificial Heart (Thomas), 11
The Evolving Challenge of Heart Failure Management (Adamson), 41
Thermo Cardiosystem II, 61f
Thiazolidinediones, 25t
Thomas, Lewis, 11
Thoracoscopes/thorascopes, 209, 210f
Thoracotomy, 208–209, 210f. *See also* Sternotomy.
Thoratec implantable VAD (IVAD), 115t, 130–131
Thoratec Ventricular Assist System (VAS), 115t, 125–126
Thromboembolic events
with circulatory support, 118
fibrillation-related, 235
intra-ventricular, 168
pulmonary, 265–270
Thyroid hormone, 286–287
Tissue flaps, 28
Tissue perfusion, 113, 114t
Tissue rejection. *See* Cardiac rejection.
Titanium plate fixation. *See* Sternal plating.
TNF. *See* Tumor necrosis factor (TNF).
Total artificial hearts, 32, 55, 56f, 115t, 133–134, 295f
Total technique for transplantation, 82, 83f
Totally endoscopic coronary artery bypass (TECAB), 109
Touhy needle insertion, 221f
TR. *See* Tricuspid regurgitation (TR).
Tracheal intubation, 282
Transesophageal echocardiogram (TEE)
anesthesiologist's use of, 284
during OPCAB, 106–107
Transmurality, 238–240
Transplantation, cellular, 307–310
Transplantation, heart
allocation principles in, 71
bicaval vs, biatrial, 218
vs. CABG, 46
donor evaluation in, 76, 78–79
hemodynamics and renal function after, 215–216
history of, 5, 192
indications for/contraindications to, 32–34, 54t, 72–75, 75–76
infection after, 89–91
pediatric, 275–277
procedures for, 80–84
prophylactic tricuspid annuloplasty in, 81, 213, 218
recipient evaluation in, 52–55, 71–76
retransplantation, 75–76
survival after, 93–94
three techniques for, 82–84
with tricuspid regurgitation, 213, 215–216, 217
vs.destination therapy, 200
Transposition of great arteries (TGA), 273–275
Tricuspid regurgitation (TR), 67–68, 116, 210–213, 216t, 217
Tricuspid valve
complex repair of, 209–212
ICD lead pressure on leaflets, 210–213
prophylactic annuloplasty of, 81, 213, 218
regurgitation through, 67–68, 116, 210–213, 216t, 217
sternal sparing incisions for, 208–209
Troponin-tropomyosis complex, 14
Tumor necrosis factor (TNF), 12
Tumorigenicity in cell transplantation, 308, 310

U
U-clip Spider, 108
United Kingdom (UK)
HF incidence and prevalence in, 41
on HF surgery indications, 42
LVAD availability in, 41
United Network for Organ Sharing (UNOS), 74–77
Univentricular circulation, 275–276
University of Chicago, 2
University of Michigan, 178–179
Urine output, 283
UW (University of Wisconsin) solution, 81

V
VAD. *See* Left ventricular assist devices (LVADs).
Valves, heart. *See specific valves*.
Valvular heart disease
circulatory support with, 114–116
defined, 24

DropBooks

in donor hearts, 79
sternal sparing incisions for, 208–209
VAS. *See* Thoratec Ventricular Assist System (VAS).
Vascular endothelial growth factor (VEGF), 310–311
Vasodilators, 16–17
Vasopressin, 99
Vasopressor agents, 99, 285–287, 292–293
VEGF. *See* Vascular endothelial growth factor (VEGF).
Vena cava
anastomosis of, 82
mobilization of, 266–267
transection of, 277f
Vena cava cuffs, 82
Ventilation, sedation during, 302. *See also* Anesthesia/anesthetic management.
Ventilation-perfusion scanning (VPS), 263
Ventricles, heart
adequate filling of, 292
aneurysms of. *See* Aneurysms.
assist devices for. *See specific devices*.
constrainment of, 19
dilatation of. *See* Dilation/dilatation, cardiac.
left. *See* Left ventricle.
remodeling of. *See* Remodeling, ventricular.
shape of, 249
single (congenital), 275
volume reduction of, 4, 18
Ventricular assist devices (VADs). *See* Left ventricular assist devices (LVADs); Right ventricular assist devices (RVADs).
Ventricular containment, 249–251
Ventricular fibrillation, 246
Ventricular pacing, 244–245
Ventricular tachycardia
after surgery, 246
surgical therapy for. *See* Ablation therapy.
Ventricular volume reduction surgery, 4, 18
Ventriculectomy
in Batista procedure, 28, 58–59
in infants, 59f
Veteran Administration Co-operative Vasodilator-Heart Failure Trial (V-HeFT I), 16–17
V-HeFT-I. *See* Veteran Administration Co-operative Vasodilator-Heart Failure Trial (V-HeFT I).
Viacor coronary sinus tensioning device, 253–254
Vitamin K, 117
VO_{2max} (maximal oxygen uptake), 26

W
Warfarin, 118
Weaning trials, 118–120, 169, 204, 269
White blood cell (WBC) immunosuppression, 84–87
Williams, Daniel Hale, 2
Wire fixation, 205, 207–208

X
Xiphisternum, 206, 208

Z
Zone of coaptation (ZC), 172, 174–177, 179f